MILK SICKNESS DRAWER 1A MOTHER NANCY HANKS

71.2009.085.05540

Hanks Family

Nancy Hanks

Milk Sickness

Excerpts from newspapers and other sources

From the files of the

Lincoln Financial Foundation Collection

How to Keep Well

by Dr. W. A. Evans

Questions pertinent to hygiene, sanitation and prevention of disease or matters of general interest will be answered in this column. Where space will not permit, or the subject is not suitable, letters will be personally answered, subject to proper limitations and when a stamped addressed envelope is inclosed. Dr. Edwards will not make diagnosis or prescribe for individual diseases. Requests for such service can not be answered.

Snakeroot Poison

GOV. SMALL has ordered a campaign against white snakeroot in his state. This is because within recent months several people have died in Illinois from drinking milk produced by cows poisoned by this weed. The name of the disease in human beings is milk sickness. In cows it is called "trembles."

White snakeroot is a weed one to two feet high and with white flowers. The weed grows on shaded, wet land, usually near the borders of pastures. Cows will not eat it, as a rule, until rather late in summer when the pastures are dry, the grass is poor, the flies are bad and the weather is hot. In these circumstances they will sometimes eat this weed rather than go out into the hot sunlight after grass.

Dr. Mark Greer reports two fatal cases. Mrs. M. B. W., after drinking milk from a sick cow, became restless and weak, developed nausea, vomiting and intense thirst. This lasted a few days, then she went into a coma, which lasted 12 days. She died.

The cow died the next day. Soon after Dr. Greer saw another family poisoned by milk in a nearby neighborhood. The mother died first. Three days later a 16-year-old daughter died. The father, three boys and a 3-year-old baby were very ill with the same symptoms. These five members of the family eventually recovered.

Mr. M. had lost 50 cows and 20 sheep from "trembles" during the time he had lived on the farm where his wife and daughter died.

Milk sickness was formerly very prevalent in the United States. Many prominent men, including Abraham Lincoln, Governor Chase Osborn and Dr. M. C. Clay have lost members of their immediate families from it. That it is again causing trouble may be due to a tendency to neglect pasture lands.

After white snakeroot had been proved to be the cause of the disease the University of Illinois undertook to find out just how poisonous the weed was. A cow, fed 12 pounds of the weed on each of five days, died in one week with "trembles." A horse fed six pounds a day for five days died on the sixth day.

A ewe, nursing a lamb, was fed a pound a day for 13 days, and died on the fourteenth day. The lamb died on the ninth day.

Dr. Greer advises the following method of preventing milk sickness:

Refrain from drinking milk and eating butter from cattle that graze in infected pastures

After July 1 advise farmers to pull the white snakeroot. If the plants have seeded, they should be pulled out and burned.

Pasture no cattle in infected fields after July 1 of each year.

6-30-26

MILK SICKNESS

MILK SICKNESS, FORMER MYSTERY ILLNESS, AGAIN CAUSES CONCERN

Ind. News 6-30-26

An old traditional sickness of mystery, which baffled the doctors of fifty and sixty years ago and which usually proved fatal, is believed to be making a "return call" in southern Indiana after having been practically forgotten except by the oldtime physicians.

A recent inquiry for information regarding the cause and treatment of milk sickness, from Dr. J. T. Oliphant, of Farmersburg, Ind., to Dr. William F. King, secretary of the state board of health, and Dr. J. E. Gibson, state inspector for the United States bureau of animal industry, has called attention to the old disease which sometimes was called "slows" or "trembles" and will probably result in an investigation of a report of one recent fatality and several serious illnesses near Farmersburg, said to be accompanied with the symptoms characteristic of the old-time milk sickness.

Little or nothing is known of a definite nature about the cause of milk sickness but many theories have been advanced and it is generally accepted that the illness is a result of drinking milk from an infected cow. Some of the old-time doctors assert the disease is the result of a cow having eaten acorns. Others say the cow poisoned her milk by eating wild parsnips or white snake root. One southern Indiana doctor a few years ago asserted that wild pigeons were the carriers of the disease or poison and offered as proof the fact that the sickness disappeared with the disappearance of the wild pigeons.

The most persistent theory is that the source of the poison is the white snake root, a plant that flourished in the woods in the days when cattle were turned loose in the wooded acres. Because the regular formulas for testing milk at the state laboratory will not show the presence or absence of such a poison the investigation has been turned over to Purdue University.

Appearance of Snakeroot Causes Alarm; Extermination Is Planned

Ind. News

County and state agriculture and animal husbandry experts are becoming alarmed over the appearance of a great quantity of white snakeroot over the state and are planning to aid the farmers in stamping out the poisonous weed. White snakeroot grows in pastures and meadows and is poisonous for cattle and horses, producing a disease known as trembles or milk sickness.

Clarence Henry, Marion county agent, said that he has been notified that three horses died of the disease in the county in the last four weeks. Not only is the weed dangerous to cattle, but persons drinking milk from a cow that has eaten it very often become fatally ill. He said that state and county authorities are planning to co-operate with farmers by organizing a campaign to stamp out the weed with the use of chemicals.

A solution of sodium arsenate or calcium chloride will kill all vegetation in the area, Mr. Henry said, and application in the fall allows the farmer to sow the field in clover the next spring so that the pasture is available for summer use.

Forage poisoning has been a serious menace to Indiana farmers for many years, it was said. Although they say that not all live stock deaths by poisoning can be attributed to white snakeroot, veterinarians generally agree that the plant is by far the most dangerous menace.

NEAR EAGLE CREEK.

The area about Eagle creek, Mr. Henry said, is most thickly grown with the plant and many of the farmers there have been forced to abandon their pastures until the plant can be exterminated.

White snakeroot grows in low woodland pastures and is rarely found in abundance in the open. There are a number of plants that resemble white snakeroot, Mr. Henry said, and identification is often difficult. The following points were given out to aid farmers in identifying the plant.

1. Roots are fibrous and matted, growing mostly on the surface of the ground.
2. Leaves are opposite, thin and the under surface has a slight luster as compared with the upper surface.
3. Each leaf possesses three main ribs or veins, which are very conspicuous on the under surface.
4. Flower clusters are white, single composite and very conspicuous.
5. Plant stands two to four feet high.

When cattle are diseased they become listless and tremble violently; their joints become stiff and the animals sometimes fall and become weak and exhausted. Horses have about the same symptoms, it was said, but with an almost entire absence of trembling. Horses often show an inability to swallow, due to paralysis of the throat muscles. Hogs are not affected by the plant, and it was suggested that hogs be pastured in meadows where the plant exists in order to exterminate it.

The main efforts of the farmers, Mr. Henry said, should be to eliminate the plant, for animals are incurable after they reach the trembling stage. The plant is shallow rooted and easily exterminated. Mowing is of little avail, for the roots will sprout. Hand pulling was advised in September when the plant is in flower, for then it is easily located. Repeated efforts year after year are sure to gain results, Mr. Henry said.

MILK SICKNESS.

PROF. A. A. HANSEN thinks there is considerable milk sickness, especially among farmers in the upper Mississippi valley. The disease is not recognized, being called ptomaine poisoning, acute gastritis, or other kinds of digestive disturbance. People do not recognize it for what it is because they have heard a lot about ptomaine poisoning and almost nothing about milk sickness. The doctors do not recognize it because they are never told about it in medical college and medical books do not mention it. If a physician should report a death as due to milk sickness, the registrar would hold up the certificate because his official list mentions no such cause.

In a report of 23 cases of milk sickness, some of which were fatal and many of which were serious, the physicians in attendance had correctly diagnosed 12. Among the other 11 were most of the mild cases, some of whom had not called in a physician.

The reason city people who drink country produced milk do not suffer from it is because they use mixed milk from a large number of cows, produced on many farms. This is another of the dangers of using milk from a single cow. The poison is carried in butter and other products as well as in the milk itself.

While it is most in evidence in August and the latter part of the summer, it may be caused by milch cows eating hay that contains the poisonous plant, and it has resulted from their eating frozen plants. When a farmer gets sick, particularly during July, August, and September, with symptoms that suggest food poisoning, Prof. Hansen thinks milk sickness should also be suspected. He should figure out how much milk he and his family have been drinking. He should send some one out to see whether the stock are sick or have been sick recently. The dry stock, cows, bulls, and steers and the sheep and calves, should be examined for evidence of trembles and diarrhea. Cows in milk stand the poison better than dry cattle because they throw off much of it in the milk. The calf may be getting some part of what the mother cow throws off.

He should next send some one to the pasture to look for white snakeroot and see if it has been grazed. The inspection should include the cut hay if any is being fed. Finally, specimens of milk, butter, and weeds should be sent to some laboratory to be examined for tremetol.

UNE: DECEMBER 9, 192

How to Keep Well

HEALTH IS WEALTH

By Dr. W. A. Evans

To the limit of space questions pertinent to hygiene and prevention of disease will be answered in this column. Personal replies will be made to inquiries, under proper limitations, when return stamped envelope is inclosed. Dr. Evans will not make diagnosis or prescribe for individual disease.

Poison in the Woods

The Strange Story of White Snakeroot, Which Science Has Finally Found Guilty of Causing Many Mysterious Deaths

By Albert A. Hansen

A FEW years ago Lynn Miller was a young bank clerk in Lafayette, Indiana. Seeing little future ahead on a salaried position, he decided to strike out for himself, and he selected a farm near Montmorenci, Indiana, as a fitting place to begin an independent career. He encountered the usual difficulties of young men starting out for themselves, but he overcame all obstacles and was apparently on the road to prosperity when a turn in his luck began with the death of a valuable horse. A short time later another horse died. It was closely followed by a third, and then a fourth, until Lynn Miller found himself in possession of a horseless farm. What had happened to his horses? He was mystified. As he pondered his loss, he recalled that each horse had died after grazing in a certain woodland pasture. One day a cow was allowed to graze in the same woods. The next day the family cat drank some of the milk, and the day following the cat was dead.

Then Lynn Miller became suspicious of his woods and appealed to the Purdue Agricultural Experiment Station for help in solving the mystery. A plant specialist was assigned to the case, the woods were explored, and white snakeroot, one of the most dangerous of poison plants, was found growing in abundance in the woods. The snakeroot was cleaned out with little difficulty, new horses were purchased, and Lynn Miller resumed his interrupted career toward prosperity and independence.

What is this mysterious plant that killed Lynn Miller's horses and poisoned the cow's milk? Behind the answer lies interesting history, many heated controversies, and the ultimate triumph of science.

THE POISONER OF THE WOODS

The flowering tops of white snakeroot, the flower that may have been responsible for the death of Nancy Hanks, mother of Abraham Lincoln.

During the days of the early settlers in Indiana, Illinois, Kentucky, Ohio, Tennessee, and western North Carolina, there appeared a new and mysterious disease that wiped out entire herds of cattle and destroyed sheep and horses by the score. The most characteristic thing about the disease was the violent trembling of its victims; and so the name "trembles" was used to designate the trouble. Wherever "trembles" was prevalent a new disease of man became evident—a disease characterized by acute intestinal paralysis and violent vomiting; hence it was called "sick stomach." Later keen observers began to suspect that "sick stomach" was passed from "trembling" cows to the human body by way of the milk; so the disease in man became known as "milk sickness."

The early literature of the Ohio Valley contained numerous references to "milk sickness," which was apparently quite prevalent, if we are to believe the statement of one writer that one-fourth of the pioneer settlers of Madison County, Ohio, died from its effects. Another authority states that over half the deaths that occurred in Dubois County, in southern Indiana, during the year 1815, were due to milk sickness, which was "also very fatal among stock." Last winter I visited Lincoln City, in southern Indiana, the burial place of Nancy Hanks, mother of Abraham Lincoln, and local tradition relates that her early death was due to milk sickness.

But what caused the mysterious disease? "Poison in the soil," said some; "Poisonous water," said others. All sorts of things were blamed, from poisonous plants to "the mystic misasma emanating from swamps"; and later, when the microbic theory was advanced, even bacteria

came in for their share of the blame. The medical profession was at odds over the whole affair, some physicians going so far as to deny the existence of "milk sickness" as a definite disease. This attitude was probably due to the fact that ptomaine poisoning and numerous digestive troubles were frequently confused with true milk sickness.

As the land was cleared and cultivated, both "trembles" in animals and "milk sickness" in man became less frequent, and the heated controversy regarding the cause of the disease gradually subsided. Interest was once more aroused when a serious outbreak of the "trembles" in the vicinity of Minooka, Illinois, caused the death of about fifty head of cattle. During the war with Germany, county agricultural agents were placed in practically every county in the United States, and one of the biggest problems that confronted the new agents in the highland counties of western North Carolina was "milk sickness" and "trembles." In that section the losses from trembles were so heavy that the development of the live-stock industry was seriously impeded.

AN UNSUSPECTING VICTIM

It has been demonstrated experimentally that the poisonous principle in white snakeroot enters the milk and undoubtedly poisons the suckling offspring through feeding.

During all this time the true cause of trembles and milk sickness was never satisfactorily demonstrated. It was not until 1914 that the mystery was definitely solved by the experiments of Marsh and Clauson, of the United States Department of Agriculture, combined with the experiments of Wolf, Curtis, and Kaupp, a short time later, at the North Carolina Agricultural Experiment Station at West Raleigh. The culprit was found to be white snakeroot, an innocent-looking white-flowered plant that grows in profusion in open woods throughout the "milk-sick" areas. Not only was white snakeroot found to be fatally poisonous, but it was also discovered that the poison was transmitted in the milk from the mother to the suckling young. Even butter made from the milk of poisoned animals was capable of killing mice. Thus the early suspicion that a poisonous plant caused "trembles," and that the poison was carried in the milk, seemed to be completely verified. The gradual diminishing of the disease as the forests were cleared and the land cultivated was also explained, since white snakeroot grows typically in the woods and is rarely found in the open, and never on cultivated land.

It must not be supposed, however, that trembles and milk sickness are extinct diseases. Far from it. The present-day prevalence of the trouble in the highland districts of North Carolina and adjacent states has already been mentioned. During the summer and fall of 1922 I found white snakeroot on a dozen Indiana farms, on which a total of 47 sheep, 19 cattle, and 10 horses died within the year, apparently from snakeroot poisoning. Numerous reports of people dying from this cause in various parts of Indiana have been made, including a recent death at Michigantown, Clinton County, and I have met a number of people who have recovered from the disease. That the trouble may be quite prevalent is not to be wondered at when it is known that white snakeroot is an exceedingly common woodland plant from Illinois and Kentucky eastward.

A series of experiments recently conducted at the Purdue University Agricultural Experiment Station proved a number of points of vital importance to farmers. In the first place, it was demonstrated that white snakeroot was fatally poisonous in the green state to both cattle and horses. It was also shown that the plant is dangerous when fed dry in hay, since so small a quantity as one pound a day fed for eleven days was sufficient to kill a horse. Since white snakeroot often grows luxuriantly along the borders of woods, it may be cut with hay, particularly wild hay. This may offer a partial solution to the mystery of poisonous hay, the cause of a great deal of trouble every year in the Ohio Valley States.

We have found a number of interesting cases of white snakeroot poisoning in Indiana. A typical example is the case of the Williams farm, near Logansport. On August 25, 1922, Mr. Creighton H. Williams, a lawyer of Fort Wayne, wrote as follows: "My mother owns some 300 acres of land about two miles southeast of Logansport. At the southern edge of the alluvial river bottom land the country rises into a higher plateau. These hills and ravines should furnish good pasture, but when I tried some years ago to secure farmers to pasture their cattle

[*Continued on page* 190]

WISCONSIN TO VOTE ON IMPORTANT FORESTRY MEASURE

A constitutional amendment will be submitted to the voters in Wisconsin in the fall of 1924 which will legalize direct state action in forestry affairs. A decision of the Supreme Court has declared state forestry activities as works of internal improvement, and it is hoped to have this disqualifying item corrected by the following forestry amendment:

"Provided, That the state may appropriate moneys for the purpose of acquiring, preserving and developing the forests of the state; but there shall not be appropriated under the authority of this section in any one year an amount to exceed two-tenths of one mill of the taxable property of the state as determined by the last preceding state assessment."

This amendment has been submitted and approved by the legislative sessions of 1921 and 1923 and must now go to the people for final ratification. Those interested in forestry in the state are now busy preparing plans so that this important matter may be brought to the attention of the voters in a forceful manner.

INDIANA STUDYING THE GROWING OF HARDWOODS

The State of Indiana has on the 2,900-acre State Forest near Henryville about 175 acres of land devoted to experiments in the growing of hardwood trees. It has been conclusively shown that direct seeding or planting of nuts in soil of the character found on the State Forest is not successful, because of their tendency to heave or freeze out. Catalpa, a tree at one time extensively planted all over the state and believed to be a solution to the timber problem, has been a miserable failure. Black locust, another hopeful in the same line, is too heavily infested with borers and in most cases does not attain post size before being broken off. It has been found useful in enriching the ground for other species, however.

Two tracts situated on similar sites, one of which was planted with tulip and the other with tulip and black locust alternately, were laid out in 1910. Measurements made of these two tracts show that in the tract where black locust had been planted with the tulip, the tulip trees are appreciably larger than in the tract where they are a pure stand. This difference is attributed to the soil-enriching qualities of the black locust.

NEW JERSEY PROPOSES TO ACQUIRE TAX SALE LANDS FOR FORESTS

With the convening of the state legislature, two important matters relating to the forestry work in the state are before the legislators for consideration. A bill providing means whereby the state may acquire tax-sale lands from municipalities for the purpose of state forests has been introduced in connection with the program for enlargement of the state forest area in New Jersey to at least 200,000 acres. The plan proposed by the bill will be of real advantage to the townships by providing a simple means of eliminating from their non-productive areas parts of the townships which have been an embarrassment and encumbrance to the townships for years, where such areas are suitable for timber-growing and recreational purposes, so that the state is justified in taking them over. It will likewise be of real advantage to the state by providing a way in which the state, at low cost, can secure idle land, for bringing back of which to productiveness and usefulness to the local community and the commonwealth the state should assume responsibility.

ERRATA

An error occurred in captioning the illustration on page 108 of the February number. The picture is that of a fur seal and not, as labeled, of the Great Northern Rhytina, or Sea Cow, the extermination of which is described in Mr. Grinnel's article.

A UNIQUE LOOKOUT TOWER

Located on Brush Mountain, in the Crater National Forest, in Oregon, this spiral stairway is of yew pegs driven into the tree, with a railing of Douglas fir, and it runs up to a height of 80 feet above ground. The picture was taken from directly under the tree, looking up.

Copies of the 1924 Index of *American Forestry* will be sent to members upon request

Poison in the Woods

[*Continued from page* 164]

on this land I was told that somewhere in these ravines is the plant causing "milk sickness," and that in years gone by many cattle were killed there, but I never found any one who was able to identify the plant." The case was investigated shortly after the receipt of the letter and white snakeroot was found growing in profusion in the death-dealing woods.

Inquiry among farmers troubled with white snakeroot poisoning revealed that the symptoms were almost uniform in practically all cases. In sheep and cattle the first indication of trouble seems to be general listlessness. The affected animals are slow of motion and are disinclined to exert themselves—a condition called the lazy or the spring-fever stage by Indiana farmers. Following the lazy stage is the trembling stage, which is characterized by spasms of violent trembling. It is sometimes alluded to as the "shimmy" stage. The "shimmying may be brought on early by driving the "lazy" animals. The joints finally become stiff, the gait becomes jerky, the victims fall and show little desire to rise. This stage is ordinarily followed by severe weakness, exhaustion, and death.

Judging from the experience of Purdue investigators, horses exhibit somewhat different symptoms than sheep or cattle. Since Dr. Craig has probably had a better opportunity to make observations along this line than any one else, I asked him to describe the symptoms to me. "The first indication seems to be slight incoordination of the muscles, especially of the hind parts, accompanied by sluggishness and marked depression," according to Dr. Craig. "The throat muscles later may become slightly paralyzed, sometimes to the extent of prohibiting swallowing. The animal finally goes down without exhibiting any signs of the trembling stage that is so characteristic in sheep and cattle. After falling, the victim rarely gets on its feet again, and death is a matter of but a few hours."

What is the cure for "trembles?" There is little that can be done to help animals in advanced stages. In the early stages, relief may be secured by eliminating the poison that has accumulated in the system. This, suggests the United States Department of Agriculture, may, perhaps, be done by the use of a purgative and by feeding laxative food, such as bran. The best course to pursue, however, is to remove the animals from the snakeroot pasture as soon as trouble develops.

Experience has demonstrated that white snakeroot is not difficult to eradicate, since the plant is shallow-rooted and yields readily to hand-pulling. A good way is to organize a band of men, assign each a strip in the infested woods, and clean the snakeroot out systematically. September is a good time to do the work, because the plants are then in flower. This has two advantages: First, the bright white flowers are conspicuous and few plants will be missed, and, second, when the snakeroot is pulled before seeds form, the removed plants may simply be dropped on the ground, since there is little danger of the plants rooting again. If the plants are large and tough, it is usually best to delay pulling until after a hard rain, when the ground is soft. The woods should be gone over a second time later on, and again the following season, in order to clean out stray plants missed during the first pulling.

Although the roots are fibrous and have the general characteristics of annual roots, one must not be deceived in this respect, since they are perennial and will sprout after cutting. For this reason, mowing infested areas is of little avail.

The identification of white snakeroot is not easy, since there are a number of closely related, but harmless, species that resemble the poisonous plant very closely. The fact that white snakeroot is practically limited to open woods, small clearings, and the borders of woods is of distinct help in identification. The dense clusters of small white flowers are also conspicuous features and the fibrous root system is somewhat distinctive. The most

One of the finest, most gracious things you could do is to tell some friend about American Forests and Forest Life. We would appreciate your courtesy and so would he.

[Reprint from the Journal of the American Chemical Society, 51, 3617 (1929).]

Tremetol, the Compound that Produces "Trembles" (Milksickness)

By James Fitton Couch

[Reprint from the Journal of the American Chemical Society, 51, 3617 (1929).]

[Contribution from the Pathological Division, Bureau of Animal Industry]

TREMETOL, THE COMPOUND THAT PRODUCES "TREMBLES" (MILKSICKNESS)

By James Fitton Couch

Received July 22, 1929 Published December 11, 1929

Tremetol is the active principle of two plants, richweed and rayless goldenrod, both of which cause the disease known as trembles. This disease is also known as milksickness, especially by the medical profession. Richweed or white snakeroot (*Eupatorium urticaefolium*) is responsible for the disease in the Central States; rayless goldenrod or jimmy weed (*Aplopappus heterophyllus*,) occurs in the Southwestern section of the United States, where it produces the same disease.

Extensive pharmacological study, the results of which have been published in other places[1] has demonstrated that the active constituent of these plants is a substance to which the name tremetol has been applied. This paper contains the results of the chemical study of tremetol.

To prepare tremetol the following procedure has been used successfully. The plant material should be fresh in the case of richweed; rayless goldenrod is still poisonous when dried but appears gradually to lose toxicity. Old dried richweed does not produce trembles. The plant is comminuted and extracted with alcohol. The solvent is distilled from the extract, best under diminished pressure, and the greenish fatty residue is extracted with boiling water as long as anything dissolves. The insoluble material is collected and thoroughly extracted with boiling 50% alcohol. The solvent is removed from this solution and the thick resinous mass that separates is allowed to cool and harden, when the watery portion of the residue may be poured off it. The resinous mass is now thoroughly extracted with boiling 30% alcohol and the solution is filtered hot from the insoluble matter. On cooling the filtrate crude tremetol ester separates. A further crop may be obtained by evaporating the alcohol from the mother liquors. The combined crops are now hydrolyzed by boiling with 5% alcoholic potash for four hours, the alcohol is distilled off and the residue is dissolved in water. The free tremetol is extracted from this solution with successive portions of ether. The ether solutions are united, concentrated to convenient volume and washed, first with dilute sodium hydroxide solution and then with water, to remove possible phenols and resin acids. The purified ether solution is now mixed with 4 volumes of petroleum ether, filtered from any precipitate and allowed to evaporate. The solution in ether and reprecipitation with petroleum ether should be repeated twice to insure purity. On removal of the solvent tremetol remains as a straw-yellow, thick oil of pleasant aromatic odor distantly reminiscent of clove and nutmeg. Should solid, waxy particles separate, the substance has not been thoroughly separated from a sterol that accompanies it in richweed

[1] *J. Agric. Res.*, **35**, 547–576 (1927); *J. Am. Med. Assocn.*, **91**, 234–6 (1928); *J. Am. Vet. Med. Assocn.*, (n. s.) **26**, 603–605 (1928). A report on rayless goldenrod is in course of publication.

and the 50 and 30% alcohol steps should be repeated. Criteria of purity are the optical rotation, index of refraction and molecular weight.

Properties of Tremetol.—Tremetol is a straw-yellow thick oil of aromatic odor. It has not been obtained in crystalline condition and decomposes when attempts to distil it are made, even when the pressure is reduced to 3 mm. It is slowly volatile in steam and appears to suffer some alteration during the process. Tremetol is insoluble in water, acids and alkalies. It is readily soluble in alcohol and the common organic solvents, less soluble in petroleum ether but readily in mixtures of that solvent with ether. It occurs in the plant in combination with a resin acid the chemical composition of which has not been determined. Tremetol readily oxidizes in the air, losing its characteristic odor and developing a rancid and acetous odor.

The analytical figures for tremetol indicate either of two formulas, $C_{16}H_{22}O_3$ or $C_{17}H_{24}O_3$, agreeing better with the latter. Molecular weight determinations, bromine absorption and molecular refractivity data agree closely with the requirements of the first formula and this has been chosen as the more likely. The high percentages of carbon and hydrogen found by analysis are considered to be due to small amounts of petroleum ether remaining in the tremetol, which cannot be driven off without decomposing the substance itself.

Tremetol absorbs four atoms of bromine per molecule at room temperature. Inasmuch as the formula indicates the presence of five double bonds, it may be concluded that the substance contains a phenyl nucleus and a side chain containing two double bonds. The function of the oxygen atoms has not been determined. Phenolic hydroxyls and alkoxyl groups are not detected by the appropriate tests. No crystalline oxime or hydrazone has been obtained. Aldehyde and carboxyl groups are absent. A study of the constitution of the substance is in progress.

Anal. Calcd. for $C_{16}H_{22}O_3$ (262.17): C, 73.24; H, 8.45. Calcd. for $C_{17}H_{24}O_3$ (274.18): C, 73.87; H, 8.75. Found: (substance from richweed) C, 73.89, 73.89, 73.33; H, 8.89, 8.58, 8.60; mol. wt., 257, 259; (substance from rayless goldenrod) C, 73.54, 73.72, 73.57; H, 8.66, 8.83, 8.94; mol. wt., 237, 262, 258. *Optical activity.* 2.9020 g. in enough alcohol to make 100 cc. rotated the plane of polarized light an average of 0.98° to the left when examined in a 10-cm. tube at 30°: whence $[\alpha]_D^{30}$ −33.82°.

Bromine Absorption.—In carbon tetrachloride solution 0.3882 and 0.4359 g. of the substance absorbed 0.4531 and 0.5466 g. of bromine at room temperature, or 1.167 and 1.254 g. of bromine per gram of substance (mol. wt. 262.17). One molecule of substance with two active double bonds reacting with four atoms of bromine requires 1.22 g. of halogen per gram; d_4^{25} 1.0787, n_D^{30} 1.5345, mol. refr. calcd. for $C_{16}H_{22}O_3$ (F_5), 76.12; for $C_{17}H_{24}O_5$ (F_5), 79.65. Found: 75.62.

Summary

Tremetol, the substance present in richweed and in rayless goldenrod, which produces the diseases known as milksickness and trembles is a straw

yellow oil, $C_{16}H_{22}O_8$, levorotatory, insoluble in water, acid and alkaline solutions, and soluble in the common organic solvents.

WASHINGTON, D. C.

CIRCULAR No. 306 NOVEMBER 1933
UNITED STATES DEPARTMENT OF AGRICULTURE
WASHINGTON, D.C.

TREMBLES (OR MILK SICKNESS) [1]

By JAMES FITTON COUCH, *chemist, Pathological Division, Bureau of Animal Industry*

CONTENTS

Trembles and milk sickness are names both of which are used to designate a disease attacking animals and persons. The disease is caused by certain poisonous plants. White snakeroot, *Eupatorium urticaefolium* Reichard, and jimmyweed or rayless goldenrod, *Aplopappus heterophyllus* (A. Gray) Blake, are the principal plants involved, but a close relative, *A. fruticosus*, of the latter has been shown (*17*) [2] to be equally capable of causing the disease. Its range, however, is more limited than that of the other two plants. These plants contain a poisonous substance known as tremetol that has been proved to be the cause of the disease. Tremetol has been obtained from the plants and prepared in pure condition by laboratory methods.

HISTORICAL REVIEW

According to tradition milk sickness was recognized as a distinct disease in North Carolina as long ago as colonial times. As the Middle West was opened to settlement the disease appeared in Ohio, Indiana, and Illinois, and eventually in other States. It was confined to the backwoods and sparsely settled regions and was never prevalent in the larger towns and cities where it could come under the observation of trained physicians, so it is not strange that it was not described in print until after the beginning of the last century. Although Thomas Ashe (*2*) in 1806 refers to a disease prevalent among the settlers along the Ohio River which, from his description, appears to have been milk sickness, the first definite account was published by Daniel Drake (*11*), of Cincinnati, in 1810. Dr. Drake's report was based on information furnished him by Thomas Barbee, a Virginia physician, who, in the course of a journey through Ohio in 1809, had discovered in the Mad River district a disease that was new to him.

Dr. Drake investigated the report during the following year and confirmed the observations. He studied the disease with the purpose of discovering its cause, pathology, and treatment and published a

[1] This circular supersedes Farmers' Bulletion No. 1593—Trembles.
[2] Italic numbers in parentheses refer to Literature Cited, p. 10.

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number of papers on the subject (*12*, *13*). Other accounts began to appear, but the printed information was confused and contradictory. Peter Smith (*22*), who was for years a traveling physician through the South and West, says:

> The yellow fever and the sick stomach I take to be the same disease, their difference being chiefly in external circumstances. They are both, properly speaking, the bilious fever.

At first the connection between the human and animal diseases was unrecognized, but it gradually became known that during the late summer and fall when "sick stomach" or "puking fever" was prevalent among the settlers there was also present the condition called "trembles" in livestock. It was observed that suckling calves sometimes sickened and died with trembles and that the dam also became sick with the same condition at the same time or soon after. An anonymous article in a Cincinnati newspaper, Liberty Hall (*1*), in 1811 describes the case of Alex. Telford and family in which the milk of four cows was suspected of conveying the disease. It soon became the current belief that the two diseases had a common cause and that the milk carried the disease from the cows to persons.

It was concluded that cows might eat some noxious substance which would pass into their milk and render this secretion poisonous to human beings. The idea spread, and soon the name "milk sickness" or "milk sick" supplanted other terms throughout the Middle West. It was thought that the flesh of animals affected with trembles would also transmit the disease, and many of the settlers abstained from meat and milk products during the autumn to avoid it.

The nature of the deleterious substance present in the poisonous milk remained obscure. Speculation as to its character was widespread and resulted in the advancement of many fantastic ideas. Poisonous dew and volatile minerals that evaporated from the earth at night, condensing on the herbage, there to await ingestion by the grazing herds; miasmata, the early conception of a germ theory; micro-organisms; various poisonous minerals, such as compounds of arsenic, copper, lead, and cobalt, as well as poisonous springs—all were advanced as explanations of the origin of the scourge. By far the most favored theory, however, and one held tenaciously from the earliest times, was that milk sickness was caused by the feeding of cows on some weed or herb that could transmit poisons to the milk.

This hypothesis was strengthened by a large number of observed facts, some of which have just been mentioned. The disease was most virulent in the late summer and early fall, particularly after a period of drought, when wholesome forage plants had been consumed and the cattle were compelled to graze on plants that they refused when other feed was plentiful. Again, cattle that were pastured in enclosed fields where weed infestation was small did not contract trembles nor did their milk cause milk sickness. It was observed that the incidence of the disease diminished as the forests were cleared and the land was brought under cultivation. Many different plants were suspected: Poison-ivy, waterhemlock, "Indian hachy", Indian-tobacco, Indian-hemp, Virginia creeper, crossvine, coralberry, marshmarigold, spurge, fools-parsley, mushrooms, and white snakeroot. It is interesting that in 1840 W. J. Barbee (*3*), of Marshall, Ill., and D. D. Owen identified the last-named plant as *Eupatorium ageratoides*, a name by which it was long classified, and made some experiments with decoc-

tions of it in which they convinced themselves of the connection of the plant with the disease. They adopted the use of sodium bicarbonate as a remedy which, in the light of our present knowledge, is a rational treatment.

Others argued that the disease was caused by parasitic fungi or by molds that grew on the plants.

Since those early days there has been a great deal of investigation of milk sickness and a large amount of literature has accumulated (*15*). The result has been that the more important facts about the disease have been determined with exactness. Its cause, course, treatment, and prevention are known, and there is no necessity for its continuance.

DISTRIBUTION AND DESCRIPTION OF THE DISEASE

Cases of trembles or milk sickness have been reported from the following States: Virginia, North Carolina, South Carolina, Georgia,

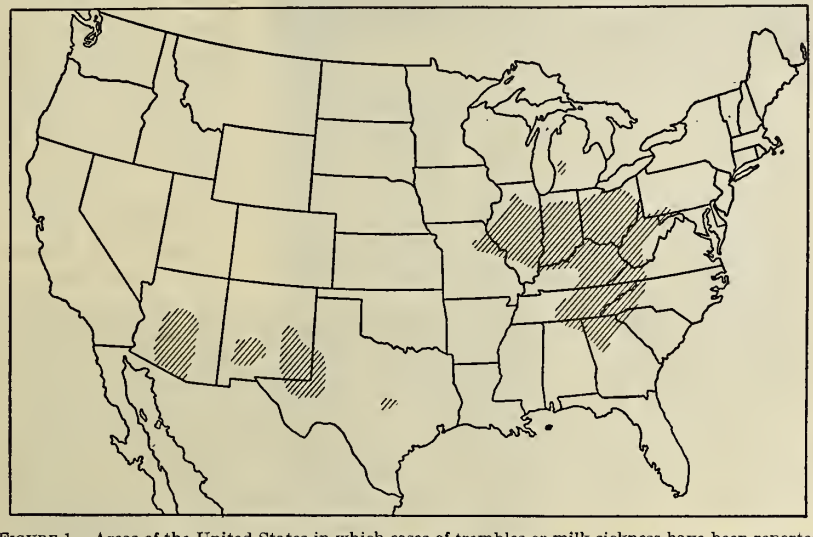

FIGURE 1.—Areas of the United States in which cases of trembles or milk sickness have been reported.

Maryland, West Virginia, Kentucky, Tennessee, Ohio, Indiana, Illinois, Missouri, Michigan, Texas, New Mexico, and Arizona (fig. 1).

The disease has been known by a number of names: Sick stomach, river sickness, tires, slows, puking fever, swamp sickness, bilious sick stomach, trembles, milk sickness, and milk sick, in the district east of the Mississippi. In the Southwest it has been called alkali disease and alkali poisoning, names that were also applied to other diseases.

The disease may be caused at any time during the life of the plants but is more common in the late summer and in early fall. It attacks many kinds of livestock. Probably no animal is immune from it. Aside from the human cases it has been observed in horses, cattle, sheep, mules, swine, chickens, rabbits, and guinea pigs. Cases have been reported also in dogs and cats.

The number of cases and the mortality cannot be stated with even reasonable accuracy. Only a few of the outbreaks are ever reported

in such a way as to be collected for medical statistics. The mortality among human beings has been estimated at about 25 percent. Wolf, Curtis, and Kaupp (*26*) collected records of 320 human cases of which 77 died. When the Middle West was being settled there was a greater prevalence of the disease on account of the lack of information about means for prevention and because so much of the pasturage was virgin forest in which white snakeroot grew abundantly. Sometimes the mortality was very high; whole villages were depopulated and many localities were abandoned by the terrified settlers. An outbreak in 1818 at Pigeon Cove, Ind., resulted in the deaths of Abraham Lincoln's mother and two of her kinsfolk, Mr. and Mrs. Sparrow (*21, v. 1, p. 30*). The early writers speak of the disease in strong terms. For example, it is "a frightful pestilence" and "a terrible malady" which "literally devastated" the country (*21*), "a very fatal disease" (*16, v. 1, p. 54*), "generally fatal to both man and beast" (*20, p. 288*). One writer states that "its terrible fatality at one period created a perfect panic in the settlers" (*14*).

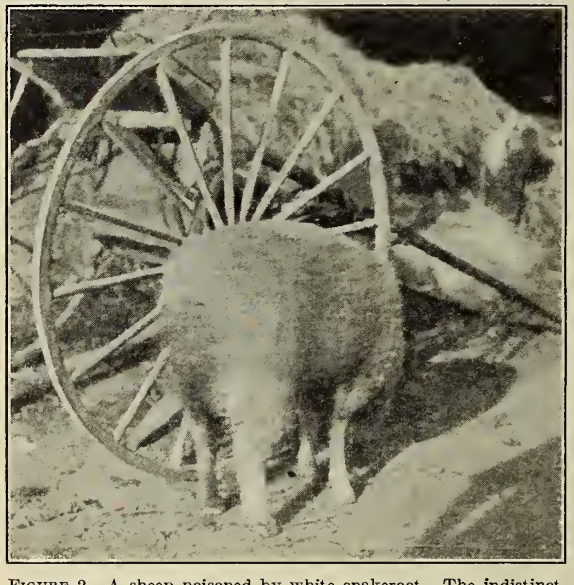

FIGURE 2.—A sheep poisoned by white snakeroot. The indistinctness of the picture of the animal was caused by its violent trembling—one of the symptoms of the disease. Note the clearness of the wheel behind the sheep.

SYMPTOMS

In human beings the first symptoms are weakness, dizziness, and loss of appetite, followed by nausea and persistent vomiting. There is pain in the region of the stomach and great thirst. The tongue is swollen and coated white, and the skin is dry. There is an odor of acetone on the breath, no peristalsis, obstinate constipation, weak pulse, slow respiration, subnormal temperature, great prostration, and frequently collapse. As the disease progresses coma develops and continues until death, which is quiet. In nonfatal cases recovery is slow. The weakness and lassitude persist for weeks, and slight exertion is very fatiguing. Relapses with fatal termination often occur during convalescence. The patient misjudges his strength and overexerts by taking a long walk or performing some laborious task about the farm, returning home to collapse and often to die within 2 or 3 days.

In animals the disease runs a course analogous to that in humans. The earliest symptom is a disinclination to exercise. The animal is depressed, does not readily rise if lying down, or moves at a slow walk when driven. With horses, cattle, and sheep, which are the animals

usually affected, this stage is followed by the characteristic "trembles" which may be the first symptom observed (fig. 2). The animal slows to a stiff-legged gait or hobble, stops with the four hoofs close together, the head hanging low and the back arched (fig. 3). The muscles of the shoulders, hips, and muzzle begin to twitch, and then a violent trembling develops during which the whole body is forcibly shaken in a longitudinal direction. In a few minutes the animal collapses (fig. 4). There is usually a strong odor of acetone on the breath and in the urine. The appetite is diminished, the temperature normal or slightly elevated, the pulse slow and weak, and the respiration during and after the spells of trembling very rapid. Constipation is generally present.

FIGURE 3.—A cow seriously affected by trembles, caused by jimmyweed; the calf in the foreground was made sick by the cow's milk.

The excretion of acetone through the lungs gives rise to a peculiar odor on the breath of milk-sickness patients. This was one of the constant symptoms mentioned by writers on the disease from the time of Drake onward. The odor was described in different ways but is so characteristic that many physicians considered it a typical symptom. Often it pervaded the house so that the physician on entering could diagnose the disease before seeing the patient. The cause of the odor is a ketosis, a condition of faulty metabolism due to the disease, a secondary manifestation of chronic tremetol poisoning. It was recognized by W. E. Walsh (*23*, *24*), of Morris, Ill., and the presence of acetone in the urine of the patients was demonstrated by R. T. Woodyatt, of the University of Chicago (*15*). The presence of acetone in the blood and urine of animals poisoned by white snakeroot or by jimmyweed has also been demonstrated (*4*). Quantities of acetone as high as 34.25 mg per 100 cc were present in the urine. In certain very mild cases no ketosis developed and these animals recovered.

FIGURE 4.—This animal was in the last stages of the disease, which was caused by jimmyweed.

PLANTS CAUSING THE DISEASE

As already stated, the cause of milk sickness or trembles is a definite chemical compound known as tremetol (*8*). The disease is

FIGURE 5.—White snakeroot, *Eupatorium urticaefolium.*

really chronic tremetol poisoning. This substance is a viscous levorotatory oil with a pleasant aromatic odor, of the composition

$C_{16}H_{22}O_3$. It is classed chemically with the higher alcohols. Tremetol is insoluble in water, acids, and alkalies and soluble in the common organic solvents, alcohol, chloroform, ether, etc. The pure substance has produced trembles experimentally in sheep (*7*).

Tremetol has been found in three plants (*5*, *9*), all of which are known to produce trembles in animals. These are (1) white snakeroot, (2) jimmyweed, and (3) the close relative of the latter, *Aplopappus fruticosus*.

WHITE SNAKEROOT

White snakeroot, *Eupatorium urticaefolium* Reichard, also called *E. ageratoides* L. in older works, is an erect perennial herb of the composite family (fig. 5). The leaves are opposite, 3 to 5 inches long, broadly ovate, pointed, sharply toothed, thin, with long petioles. The small heads, each containing from 10 to 30 tiny white tubular flowers, are arranged in terminal compound corymbs and appear in late summer and early fall. The plant grows from 1 to 4 feet in height. It occurs widely throughout the eastern part of the United States and as far west as Minnesota, Nebraska, Oklahoma, and Texas. It is most commonly found in open woods in moist locations but often grows in the open in cleared ground.

It is commonly known as white snakeroot throughout the Middle West, but has also been termed richweed (*6*), white sanicle, Indian sanicle, deerwort, boneset, poolwort, poolroot, squawweed, whitetop, stevia, and snow thoroughwort.

FIGURE 6.—Jimmyweed, *Aplopappus heterophyllus*.

JIMMYWEED OR RAYLESS GOLDENROD

Jimmyweed, *Aplopappus heterophyllus* (Gray) Blake, also called *Isocoma wrightii* and *Bigelovia rusbyi*, is a stout, erect, tufted perennial herb (fig. 6) belonging to the composite family. The plant is usually from 1 to 2 feet tall but may reach 4 feet under favorable conditions. The alternate leaves are from ¾ to 2½ inches long by ⅛ to ¼ inch wide. The numerous small yellow heads are closely clustered at the top of the stem and branches, and each contains from 7 to 15 tubular disk flowers. It grows from southern Colorado to western Texas, New Mexico, and Arizona, and extends southward into Mexico.

APLOPAPPUS FRUTICOSUS

Aplopappus fruticosus,[3] a species having no well-known common name, is similar to *A. heterophyllus*. The principal distinction is that in *A. fruticosus* the leaves are divided into 2 to 6 pairs of very narrow

[3] This description has been furnished by S. F. Blake, senior botanist, Bureau of Plant Industry.

lobes, whereas in *A. heterophyllus* the leaves are entire or merely toothed. *A. fruticosus* occurs in Arizona, Texas, and Mexico.

TRANSMISSION THROUGH MILK

Independent observations by a number of investigators have established the fact that milk sickness or trembles can be transmitted through the milk of cows or other lactating animals that have received tremetol internally either as such or by feeding on plants that contain it. Suckling calves and lambs have become sick when the dam has eaten white snakeroot or jimmyweed (rayless goldenrod) (*19*), and the symptoms exhibited by the suckling animals have not differed essentially from those shown by adult animals with trembles (fig. 7). Cream and butter from the milk have also been incriminated as conveyors of the poison. Since butter may be stored for several months before use it is possible that outbreaks of milk sickness due to poisoned butter may occur during the winter months at a time when the plants which produced the poison have been killed back by frost.

FIGURE 7.—This calf was poisoned by the milk of its mother; the cow was poisoned by white snakeroot.

Milk capable of causing the disease may be secreted by an apparently healthy cow. There are several cases recorded by physicians in which persons who drank the milk became sick and some of them died before the cows showed any symptoms of trembles. R. G. Wilkinson (*25*), of Greeneville, S.C., reports two series of cases in which the cows showed no symptoms until from 1 to 21 days after the patients became ill. M. B. Culpepper (*10*), of Carlsbad, N.Mex., records an outbreak of 6 cases in 1 family in which the cow did not sicken at all although her suckling calf died of trembles.

Outbreaks of milk sickness have usually occurred on isolated farms where the family has been drinking milk from one, or at most, a few cows. The disease has never been recorded as due to milk from creameries and is unknown in the cities and larger towns. Unlike a micro-organism, tremetol cannot propagate itself in milk and there appears to be little danger from mixed milk supplies for large communities from this source.

MEAT FROM ANIMALS DEAD FROM TREMBLES

There have been many field observations that the flesh of animals which died from trembles is capable of transmitting the disease. However, it has been impossible to confirm these reports by labora-

tory investigations. Careful feeding of such flesh to cats and dogs by Jordan and Harris (*15*), Wolf, Curtis, and Kaupp (*26*), Marsh and Clawson (*18*), and the writer has been without effect. Considered from a point of view of dosage, it is unlikely that enough tremetol could be stored in the flesh to furnish a toxic dose even when such flesh is eaten for a reasonable period.

Although tremetol is a cumulative poison, indications are that the body is able to metabolize a certain quantity of it and to convert it into harmless products. Consequently there is a certain minimum dose that must be taken each day for poisoning to result. It is unlikely that enough tremetol could be obtained from contaminated meat to supply this minimum dose.

Since cows can secrete the poison in their milk the above considerations furnish an explanation why lactating cows are unaffected when steers and dry cows in the same herd and on the same pasturage are affected by trembles.

REMEDIES

The most important procedure in treating a case of milk sickness is to remove the cause. All milk and butter should be obtained from reliable sources. Since milk-sickness patients cannot retain solid food the practice is to put them on a milk diet. If the nature of the illness is not recognized the milk served may be from the same source as that which caused the illness, and the unfortunate patient is further poisoned by the measures taken to relieve him. Immediate change of milk and butter supplies is imperative.

Medical treatment of milk sickness consists of supportive measures, combating the ketosis, and relieving the constipation. The use of enemas of glucose and sodium bicarbonate is a recognized procedure. Complete rest is necessary and during convalescence no extensive exertion should be allowed. Relapses are common and the mortality is high.

Remedies for trembles in animals consist in rest and general supportive treatment. If ketosis has not become marked the prognosis is good. A drench of sodium bicarbonate 3 or 4 times a day and a large dose of Epsom salt are recommended. Feedings of oats and a liberal supply of drinking water are of benefit.

PREVENTION

Milk sickness or trembles may be completely prevented by keeping livestock away from patches of white snakeroot in the East and jimmyweed and *Aplopappus fruticosus* in the Southwest. White snakeroot may be pulled up before seeding and piled out of reach of animals. In this way pastures may be cleared and all danger removed. Since the seeds may remain viable for some years the pastures should be inspected each year and all seedlings destroyed. Where eradication is not practicable the patches of weed should be fenced off and the livestock kept out. Jimmyweed may be dug out of pastures. The plant will be killed if it is cut off about 3 inches below the surface. This work should be done before the plant goes to seed; otherwise the dug plants should be burned to prevent reseeding. Both are perennial plants and mowing will not kill them.

SUMMARY

Milk sickness or trembles is a disease that attacks persons and lower animals alike. It is due to a poisonous substance, tremetol, present in certain poisonous plants.

In the eastern portion of this country white snakeroot is the plant that carries tremetol. In the Southwest, jimmyweed and a closely related plant, *Aplopappus fruticosus*, furnish the poison.

The poison is secreted in the milk of animals that have grazed on these plants and such milk is capable of causing the disease in persons and suckling animals.

The disease can be prevented by keeping livestock away from the plants either by fencing off the areas where the plants grow or, better, by destroying the plants.

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White Snakeroot Poisoning

Circular
436

University of Illinois
College of Agriculture
Agricultural Experiment
Station and Extension
Service in Agriculture
and Home Economics

(See color plate, page 4)

MILK SICKNESS in man and "trembles" in farm animals occur each year in Illinois. These two diseases are really identical and are caused by a toxic substance known as tremetol, a constituent of white snakeroot, a plant widely distributed thruout the wooded sections along rivers in Illinois. Milk sickness occurs as a result of consuming milk or meat products from animals that have been eating white snakeroot. Extreme care should therefore be exercised in keeping food-producing animals away from fields where white snakeroot grows.

Trembles and milk sickness are more prevalent during the late summer and early fall months than at other times of the year. This is particularly true after drouth, when pastures are short and animals are forced to feed on plants which they ordinarily would refuse.

To prevent these distressing and often fatal diseases in farm animals and in man, the white snakeroot plant must be exterminated or animals kept out of pastures in which it is growing.

Urbana, Illinois May, 1935

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H. W. MUMFORD, *Director*, Extension Service in Agriculture and
Home Economics, University of Illinois.

White Snakeroot Poisoning

By Robert Graham and V. M. Michael[1]

WHITE SNAKEROOT or Eupatorium poisoning, commonly called "trembles," is primarily a disease of cattle, sheep, and horses, which may occur also in man as the result of drinking milk or eating meat or milk products from affected animals.

Altho the poisonous character of white snakeroot has been recognized for many years,[2] the plant is still abundant in many woodland pastures of Illinois.[3] Many owners choose to protect their animals by avoiding the use of infested pastures rather than by exterminating the plant. Others have not been aware of the presence of the plant until their animals became affected with the disease.

Serious outbreaks of white snakeroot poisoning in man and animals have led to feeding tests with the fresh plant by the U. S. Bureau of Animal Industry and by several state experiment stations, including the Illinois Station. These tests have proved definitely the poisonous nature of the plant and its potential danger to man and animals.

History of Poisoning in One Illinois Township

How white snakeroot may affect men and animals in a community over a long period of time is illustrated by the following history of outbreaks of trembles and milk sickness in Button township, Ford county, from 1862 to 1922, supplied by Dr. E. C. Park, of Paxton, Illinois:

"At intervals of every few years for the past sixty years or more, [1922] cases of milk sickness in persons and trembles in livestock have occurred in Button township. This township is an uneven country of loamy soil, small streams and wooded pastures in which *Eupatorium urticaefolium* (white snakeroot) grows in abundance.

"In two of the pastures in Button township, the plant grows in such abundance as to exclude almost all other vegetation. Stock pastured in

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[1]Robert Graham, Chief in Animal Pathology and Hygiene, and V. M. Michael, First Assistant.

[2]The poisonous character of white snakeroot and the possible relation of trembles in domestic animals to milk sickness in man were suspected by a few investigators as early as 1830. The prevailing opinion at that time, however, did not agree with these suspicions, and lack of general knowledge of the causative factor delayed a systematic effort to destroy the plant or to keep animals away from infested pastures.

[3]White snakeroot was found in 11 of 13 counties investigated in Illinois in 1926.

these fields are forced to eat the weed or go without sufficient food. Most of the wooded land has been cleared and cultivated until there are only a few of the pasture fields in which the weed will grow. As a result, in recent years the cases of milk sickness have been traced easily to two or three of the inclosed pasture fields in the community and all of the cases which occurred in the last four years to certain pastures on one or two farms. It was the practice in years gone by, when the stock would sicken and die of the disease, to transfer it to some other pasture, or fence off the portion of the field where the snakeroot grew thickest. A temporary fence, a remnant of the effort to check the disease, still remains on one farm.

"Some twenty years ago a resident of one of these farms died of milk sickness. In 1922 two children living on the same premises suffered severe attacks of the disease which lasted several weeks and were followed by a long and tedious convalescence."

An inspection of the cattle in the 1922 outbreak on this farm revealed two milk cows that were emaciated, but symptoms of trembling were not observed. Simultaneously with the illness of the children and the emaciated condition in the cattle, two horses in the same pasture died after displaying symptoms suggestive of Eupatorium poisoning.

Each year similar outbreaks of white snakeroot poisoning occur in late summer and fall in some locality in the state, emphasizing the urgent need for prevention of this disease.

White Snakeroot a Slender Perennial

White snakeroot (*Eupatorium urticaefolium*) is a slender, erect, perennial herb which grows from 1 to 5 feet high. The leaves are opposite each other, 3 to 5 inches long, broadly ovate, and have sharply toothed or serrated edges. The upper surface is somewhat dull, while the under surface possesses a slight luster. Each leaf has three main veins, which are prominent on the under surface and which extend from the base of the leaf and give off many branches. The leaf stalks are about one-fourth to one-half as long as the leaf. In the late summer the small white flowers of the plant appear as compound clusters, having eight to thirty flowers. The roots are coarsely fibrous and usually shallow. Pastures in heavily infested woodland areas present an attractive appearance and it is not uncommon for persons to select clusters of white snakeroot flowers for home decoration. The diagrammatic illustrations in Fig. 1 show the characteristic features of the plant.

White snakeroot grows profusely in the damp rich soil of woods, swampy areas, shady ravines, and in groves along streams. Altho pre-

ferring shady places, it has been found on cleared hillsides and somewhat sparingly in orchards and orchard pastures over a wide area of the more highly cultivated agricultural sections of the state.

Closely related nonpoisonous plants of the Eupatorium genus grow abundantly in open pastures and are often mistaken, upon casual ob-

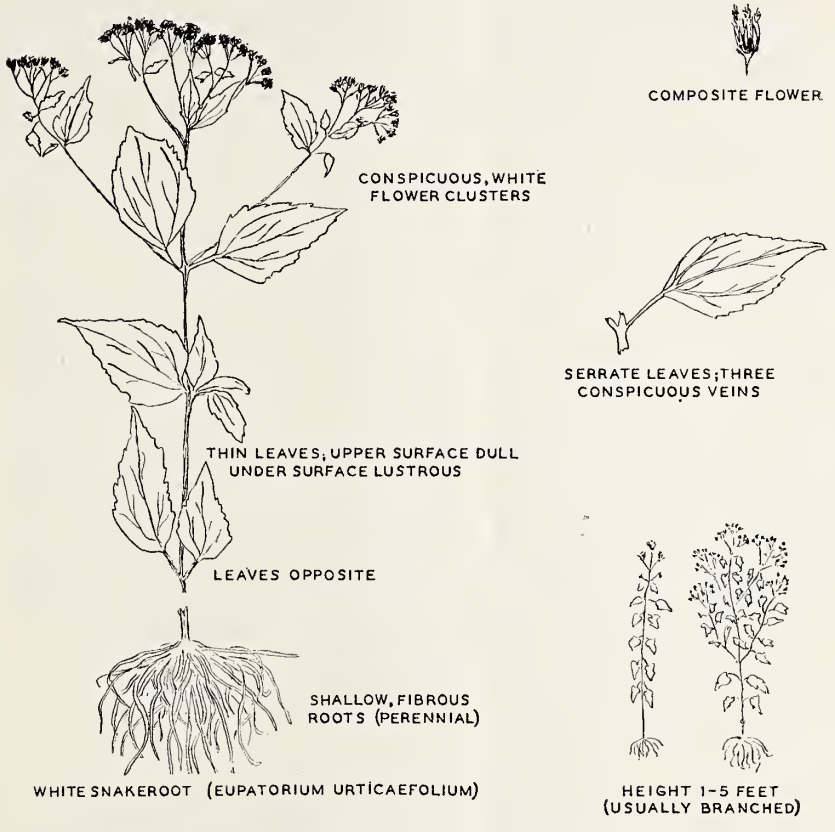

Fig. 1.—Characteristic Details of White Snakeroot

White snakeroot (*Eupatorium urticaefolium*) is a slender, erect perennial herb which grows from 1 to 5 feet high. In the late summer the small white flowers appear as compound clusters, having 8 to 30 flowers. The roots are coarsely fibrous and usually shallow.

servation, for the poisonous type. The nonpoisonous member of this genus, which is prevalent in Illinois, can be distinguished by its narrower leaf. *Specimens of suspected plants may be sent to the Agronomy Department, University of Illinois, Urbana, for identification.*

Tremetol Is the Active Principle in Poisoning

Three toxic substances have been isolated from green *Eupatorium urticaefolium* (white snakeroot). Two of these, a volatile oil and a resin acid, do not produce "trembles" in animals and have no relation to milk sickness. The third, tremetol, is held responsible for both.[1]

Tremetol ($C_{16}H_{22}O_3$) is an aromatic straw-yellow oily liquid which is insoluble in water, acid or alkali, but soluble in common organic solvents, such as alcohol, ether, chloroform and benzene. It may be altered by heat or chemical reagents and when so changed loses its poisonous properties. Drying also rapidly destroys tremetol, and completely dried plants are rarely capable of producing trembles. Tremetol is a cumulative poison; while no ill effects, or only slight symptoms, are observed if less than the lethal dose is ingested, several small amounts at various feedings may produce typical poisoning.

Tests for Tremetol.—The nonpoisonous plants of the Eupatorium genus have been shown to contain no tremetol, whereas the poisonous plant does contain tremetol. The following test has been described by Couch[1] for the detection of tremetol:

> "The suspected material is shaken with purified petroleum benzin and the solution is floated on the surface of 2 or 3 cubic centimeters of concentrated sulfuric acid in a dry test tube. If tremetol is present, the interface or surface between the two liquids is colored red. When the two liquids are mixed by shaking the tube, the petroleum benzin solution becomes a transient red, while the acid layer acquires a cherry red, more or less intense according to the amount of tremetol present. This color should develop as soon as the solutions are mixed. If only minute amounts of tremetol are present, a yellow or orange color may be the result."

The presence of tremetol can be confirmed by feeding the suspected material to guinea pigs.

Varying Susceptibility of Animals

In studies conducted at the Illinois Agricultural Experiment Station with domestic animals, marked variations occurred in susceptibility of the individual animals to white snakeroot poisoning. Some died after eating amounts of the plant equivalent to only 1 to 2 percent of their body weight; other animals, especially the guinea pigs, ate the equivalent of 15 to 18 percent of their weight before death ensued.

Fresh and dried snakeroot fed experimentally to horses, cattle, sheep, and guinea pigs frequently produced symptoms of white snake-

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[1]Couch, J. F. The result of richweed poisoning. Jour. Amer. Med. Assoc. 91, 234-236. 1928.

root poisoning, altho some of the animals, particularly the milk cows, did not succumb to an acute type of the disease. Cattle and guinea pigs especially seemed to exhibit a tolerance to the poisonous constituent of the plant, altho some of the guinea pigs refused to eat the fresh leaves in amounts sufficient to produce death. Hogs are highly resistant and seldom suffer from white snakeroot poisoning.

Aqueous and alcoholic extracts of white snakeroot, as well as the expressed sap and the residue of alcoholic extracts, when fed to guinea pigs and goats, did not consistently produce illness and death, altho an occasional death suggested that the poisonous property of the plant was present in the extracts. A tolerance of animals to these extracts comparable to their tolerance to the feeding of the fresh plant was observed.

When twenty-two pigs were fed carcasses of a cow and ewe which had died of white snakeroot poisoning, symptoms suggestive of poisoning were produced in two of them.

Symptoms and autopsy findings in a nursing lamb, the mother of which had been fed fresh white snakeroot, indicated that the milk was the source of the poison; but experimental animals receiving milk from cows eating the plant were not consistently poisoned. Milk, milk serum, and casein from cows fed white snakeroot injected subcutaneously into guinea pigs in amounts of 2 cubic centimeters frequently failed to induce symptoms of white snakeroot poisoning. Butter prepared from milk of cows pastured on white snakeroot did not produce illness when fed in small amounts (.5 gram) to guinea pigs.

Symptoms of White Snakeroot Poisoning

White snakeroot poisoning appears only in pastured animals—horses, cattle, and sheep being the ones usually affected. White snakeroot is not well liked by grazing animals, but during periods of drouth, or if a field is overpastured, they may be forced to eat it. If the plants are numerous, the animals may eat the leaves from time to time even tho pasture grass is abundant (Fig. 2).

Attempts to disclaim the poisonous character of white snakeroot may be due partly to the fact that symptoms somewhat resembling those of poisoning by this weed may result from other causes. The symptoms described in this circular, however, are based upon experimental work which proved conclusively the poisonous character of the weed. The symptoms exhibited by the experimental animals could not be distinguished from those appearing in animals that have had access to the plant in pastures.

Cattle.—Cattle grazing on pastures infested with white snakeroot often become chronically affected. In this chronic form the disease is marked by sluggishness and fatigue following exercise. The animal is listless, and when forced to walk, the movements are slow and stiff. One method of diagnosing suspicious cases consists of forcing the animal to move and observing the tone of the voluntary muscles. A

FIG. 2.—WHITE SNAKEROOT IN A WOODLAND PASTURE SHOWING HOW PLANTS WERE EATEN BY CATTLE

Altho occasionally seen in open fields, white snakeroot is usually found in woodland pastures. The plants shown above have been stripped of their leaves by cattle. Animals valued close to $30,000 died from white snakeroot poisoning, over a period of six years, while grazing in the above pasture.

trembling of these muscles often indicates that the animal has white snakeroot poisoning. This trembling, however, usually disappears after a rest.

Severely affected cattle are constipated, lose appetite and weight, become increasingly weak, and finally are unable to stand. The animals may sink to the ground and remain lying for hours or days, and when helped up often show marked symptoms of trembling, standing with body arched and hind feet placed close together well under the body. Respiration is difficult, and the breath has a peculiar, pungent, fetid odor due to acetone. Frequently profuse nasal discharges are observed. Animals in this stage usually die. Not all the cattle in a herd, even tho kept under the same conditions, develop the disease, while the severity of the symptoms generally varies among animals. Three stages of the disease in cattle are illustrated in Fig. 3.

Horses.—The disease runs a more rapid course in horses than in cattle. Affected horses often die within two or three days after the symptoms of illness appear. The first symptoms are an unsteady gait, suggestive of weakness, and difficulty in swallowing, accompanied

frequently by excessive slobbering and distressed and heavy breathing. The breath of affected horses has the same pungent odor that is noticeable in cattle. The animal appears gaunt and dejected, loses weight rapidly, and moves reluctantly. These symptoms usually are accompanied by constipation and by trembling of the large body

FIG. 3.—TYPICAL SYMPTOMS OF WHITE SNAKEROOT POISONING

Animals in the first stage of white snakeroot poisoning (*A*) become weak, tremble, and lie down frequently. *B* shows a calf in the advanced stage, in a semiconscious state. The calf shown in *C* is suffering from acute poisoning. The closed eyes, semicomatose attitude, weakness, emaciation, and trembling are characteristic of the last stage of the disease.

muscles, altho the trembling generally is intermittent and not so marked as in cattle and sheep. Death generally follows in a few hours after the affected animals "go down."

Sheep.—Symptoms observed in sheep generally resemble those of cattle. One of the first symptoms is loss of appetite and grinding of the teeth. The animal becomes sluggish and disinclined to move. A trembling of the muscles may be especially noticeable following exercise, tho affected sheep usually lie quietly. When helped up, the animal stands with the feet spread apart laterally and the hind feet placed

well under the body. The back is bowed, the neck outstretched, and the head lowered (Fig. 4). After two or three days, or in the latter stages of the disease, the animal becomes comatose and may lie on its side until death occurs. When coma starts, a frothy discharge from the nostrils is not uncommon.

FIG. 4.—SHEEP POISONED WITH WHITE SNAKEROOT

Sheep in the late stages of white snakeroot poisoning assume a sleepy attitude.

Hogs.—The symptoms observed in hogs are similar to those in cattle and sheep. The animal is listless and remains in a prone position unless urged to rise. There is no marked decrease in appetite. The animal stands with the hind feet well under the body, eyes half closed, head lowered and back bowed. In the initial stages of the disease, the hind legs appear stiff; later the stiffness may spread to the front legs. After the pig stands a few minutes, trembling begins and becomes so severe that the animal falls on its knees or sits on its haunches, then falls to the ground. Coma precedes death.

Guinea Pigs.—The disease is first evidenced in guinea pigs by their refusal to eat. The animal becomes listless and crouches in the cage with eyes half-closed. The hair becomes rough. Muscular tremors, altho present, are not especially noticeable. Complete lack of muscular coordination and stupor precede death (Fig. 5).

Man.—The onset of the disease in man is gradual and is characterized by a restless, weak, and languid feeling. Later excessive vomit-

ing occurs, accompanied by loss of appetite and obstinate constipation. The peculiar fetid odor of the breath is considered diagnostic. Respiration may be labored, the pulse weak, and the temperature abnormal. Severe cases sometimes resemble typhoid fever. The patient may be delirious, and coma generally precedes death, which may follow two days to three weeks after the first symptoms. Patients who recover seem to have lasting debility. One attack of the disease produces no immunity to subsequent poisonings.

Fig. 5.—Guinea Pigs Suffering From White Snakeroot Poisoning

These pigs ate approximately five leaves of white snakeroot plant each day for four successive days. They were photographed on the fifth day a few hours before death occurred.

Prevention of White Snakeroot Poisoning

Avoid Food Products From Sick Animals.—Prevention of milk sickness in man depends upon the avoidance of milk, meat, and milk products from animals that have had access to white snakeroot, for tremetol may be transmitted thru the milk of cows which show no definite symptoms of poisoning. Since the toxic principle is destroyed only very slowly at the temperature of boiling water, milk pasteurization is of little value in destroying the toxin. In a general milk supply or in creamery butter, however, the toxic principle is so diluted that it may become harmless. The disease appears to result from the *continued* use of milk or butter from affected animals, rather than from the occasional consumption of a small amount in a mixture of milk from diseased and healthy animals. The occurrence of the disease in rural families and its absence in cities is doubtless explained in this manner.

A careful observation of the herd from August to November should enable the owner to detect obscure cases. Likewise inspection of animals and pastures in localities where white snakeroot is prevalent is recommended.

Exterminate Weed.—The clearing of underbrush and the cutting of trees to permit ample sunlight discourages the growth and spread of white snakeroot. Cropping is also an aid in checking the growth of this plant. It has been noted that the plant increases on partially cleared land and disappears after cultivation. If the pasture is small and the infestation limited, white snakeroot, which has very shallow roots, can be eradicated with little effort by pulling. This should be done in August or September, when the flowers are in bloom, and repeated in October. After the plants have been pulled and allowed to dry, they should be burned in order to destroy the seeds. Pulling and burning should be repeated each fall until the plant is eradicated. Since white snakeroot is a perennial, it cannot be eradicated by cutting.

If large pastures are heavily infested with white snakeroot, making it impractical to pull the plants, it is advisable to move the stock to new pastures about the first of July and keep them there until December 1, or until the pastures are freed of the weed.

No Satisfactory Treatment for the Disease

The treatment of animals and man for white snakeroot poisoning is far from satisfactory. For animals suffering from white snakeroot poisoning, veterinarians recommend purgatives such as castor oil or soybean oil, with repeated doses of stimulants. It should be borne in mind, however, that partial throat paralysis may occur, and the oral administration of drugs may therefore be a dangerous procedure. Each case should be treated individually under the direction of a veterinarian. When symptoms of the disease appear, the animals should be moved promptly to noninfested pastures, and as a precautionary measure should be given laxative food for ten days to two weeks.

In human cases of Eupatorium poisoning an early diagnosis is essential to recovery. Whenever symptoms similar to those of white snakeroot poisoning develop within two to fifteen days after drinking milk or eating meat or dairy products from a herd which has had access to white snakeroot, a physician should be called immediately and treatment given. The progress of the disease is usually rapid and mortality high; in one state 24 percent of the reported cases ended in death.

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WHAT IS SCIENTIFIC PROOF?

The Commonest Mistake . . . What the Real Method of the Scientist Demands . . . Hard-boiled, Cold, Rigorous Logic . . . Two and Two are Not Nine

By T. SWANN HARDING

HAVING been trained in science I have what I find to be a particularly bad habit of saying, "But that is not true scientifically." Scarcely anything is more annoying to a person's habitual associates, especially to his wife, than that habit. I am therefore asked in return, and sometimes with scant courtesy: "Then what is scientifically true? How do you prove anything by science? What sort of evidence would convince a scientist?"

and tell-tale flaw in it that gives the whole thing away.

Can we truly say that, because of these things, therefore the child died of arsenic poisoning? We can not. Why? Because the accused apples were never apprehended. They were never analysed and shown to contain dangerous quantities of arsenic. Indeed the apples that were shipped into the state concerned at the time the girl was eating hers were, according to the record, well within the tolerance for arsenic spray residue. Moreover, some persons are very sus-

A heifer afflicted with trembles, caused by eating certain plants

ceptible to arsenic and may be poisoned fatally by minute quantities of this substance, derived from two or more sources, that would have no apparent effect upon normal individuals.

Other questions might be asked. What about the possible effects of this sudden and abruptly started habit of eating five apples a day? Isn't that rather a considerable change in diet for a young girl? Might not that factor alone affect her health? Again, might not a few of the apples eaten have by accident contained really excessive quantities of arsenic or, what is more likely and far more dangerous, lead spray residue, which sickened the child? For not many apples could have been so affected, since dozens of other children ate them and went unharmed. Finally, the child may have made up her total minute toxic dose of this drug by accumulating other small quantities of it in other foods.

It is very easy to put 2 and 2 together and make 9 in such instances. Two hasty and ill-informed writers recently put 2 and 2 together and called it 100,000,000 and began, in their hysterical dreams, to imagine that we all were guinea pigs. But, aside from all other considerations, it is the devil's own job to prove that persons are afflicted with arsenic or with lead poisoning. It takes weeks or even months of the most careful laboratory investigation to do this.

Consider lead poisoning, for example. Certain patients enter a certain clinic, assumed to have lead poisoning. Very soon the laboratory workers burst out into a song of joy because they have found "excessive" quantities of lead in the urine of all these assumed victims of lead poisoning. The case was "proved," indeed, until some skeptic asked: "What is an 'excessive' quantity of lead in the urine?" Nobody had thought of that, so they went to work again, still thinking they had found an infallible means of easily diagnosing lead poisoning.

But they next discovered just as much lead in the urine of other sick people in the clinic as in that of those supposed to have lead poisoning. Then they found lead in similar quantities in the urine of several "normal" people who had merely accompanied their sick friends to the clinic. Last of all they found no greater quantities of lead in the urine of certain cancer patients who had been treated with nearly toxic doses of lead, than in the urine of "normal" people. So the theory simply blew up, and a new way of proving that certain people have lead poisoning must be devised.

TO illustrate what scientific proof really means, suppose we take two cases in which the scientists were more successful. Lincoln's mother died of a dread ailment called "milk sickness." That offers us an excellent example. What caused milk sickness? Until scientists in the United States Bureau of Animal Industry recently found out, we did not surely know. The disease was long a violent scourge, with a 25 percent mortality, and it has been known in this country since colonial times.

It was described by physicians as early as 1806 to 1810. One of them wrote: "The yellow fever and the sick stomach (another name for milk sickness) I take to be the same disease, their difference being chiefly in external circumstances. They are both, properly speaking, the bilious fever." This was a blind essay in classification which, however, offered little real enlightenment. But very gradually it came to be seen that sick stomach or milk sickness (also puking fever to some) was most prevalent in late summer or early fall. At this same time the disease called "trembles" was prevalent among cattle. Hence it looked as if the cows consumed some poison at this time and passed it along to the humans who drank their milk.

What could that deleterious substance be? Some said it was poisonous dew or volatile mineral substance that evaporated from the earth at night, condensed on the herbage, and awaited the cattle. Others attributed it to "miasmata," the illegitimate grandfather of germs and the germ theory of disease. Others declared some sort of micro-organisms to be guilty, while others still attributed "trembles" to poisonous combinations of silver, copper, lead, or cobalt found in certain springs. There were those, however, who persisted in believing that the disease appeared when cows ate certain herbs.

Next it became necessary to say what

these herbs were. The following came under suspicion: Virginia creeper, Indian hachy, Indian tobacco, Indian hemp, crossvine, Indian currant, marsh marigold, spurge, fool's parsley, mushroom, and wild snakeroot. As early as 1840, decoctions of wild snakeroot were made by two physicians who convinced themselves that this plant caused "trembles" in cattle, and who treated it with sodium bicarbonate, the recognized remedy today. But many still held then that fungi, or mold on plants, made the cattle ill.

The disease caused in humans, the milk sickness, was a frightful pestilence; it literally devastated parts of the country. The odor of acetone was strong on the breath of victims, indicating faulty metabolism with what is called "ketosis." About 1909 it was demonstrated that there actually was acetone in the urine of these patients. Finally, organic chemists went to work on some of the plants that had so long been supposed to cause trembles in cattle whose milk gave human beings milk sickness. In wild snakeroot or milbane, in rayless goldenrod, and in a close relative of the latter called *Aplopappus fruticosus*, Couch, of the Bureau of Animal Industry, in 1928-1929, found a viscous oil with a pleasant, aromatic odor, of the composition $C_{16}H_{22}O_3$, which classifies chemically with the higher alcohols, and is insoluble in water, acids, and alkalis, but is soluble in most organic solvents.

THIS compound Couch called "tremetol" because, when he administered it to sheep, he could produce "trembles" in them experimentally. It was also shown that the milk of animals which consumed tremetol, either direct or in one of the poison plants, could cause milk sickness in human beings. The meat of such animals remained unaffected and was fit for food. The tremetol passed into the milk. If grazing animals are kept away from the three plants mentioned they never become afflicted with trembles; consequently their milk can not cause milk sickness in human beings and the whole problem is solved scientifically.

It is solved because one factor was isolated. This one factor could then be varied while all other factors were held constant. This was no matter of having 10 groups of 50 people each use different gargles while they dressed, exercised, worked, ate, played, breathed as they pleased, and then trying to conclude that, when all these many factors varied, the one factor, the gargle, prevented or cured their colds. Instead, a definite organic chemical was prepared from plants causing trembles. It was purified. When fed it would cause trembles to a greater or lesser extent depending on the quantities fed.

When human beings drank the milk of cows that had developed trembles from consuming tremetol they got milk sickness. That was the one important factor. But the one factor of supreme importance is not always so easy to find. I will give one more instance to demonstrate this. It concerns a disease of pecan trees called rosette. This disease makes a pecan tree simply curl up and die, and is no end disastrous to the profits of its owner. So scientists from the Bureaus of Plant Industry, and of Chemistry and Soils, began experimenting with various available dips and sprays to prevent or cure the disease, if possible.

A pecan tree "curling up and dying" from rosette. It took a lot of sherlocking to find the cause of it

Finally they found that by dipping the rosetted pecan leaves in a solution of iron sulfate they were able to prevent rosette on young leaves and to improve the condition of older diseased leaves. They therefore sprayed pecan trees the next season with iron sulfate solution, practically certain that this one factor would prevent the development of the disease. But their case was not proved. Rosette appeared just the same. So they checked back on what they had done the previous year.

The analysis of the iron sulfate solution then used disclosed the presence of a considerable quantity of zinc. Where did that come from? Why wasn't there zinc in the iron sulfate solution they were using now? Because last year the solution had been mixed up in galvanized buckets; this year it had been mixed in glass. So-called galvanized water buckets contain zinc. Possibly some of the galvanic coating of the water buckets dissolved in the iron sulfate solution, and perhaps that zinc was the factor preventing rosette. Result? Zinc sulfate was tried; it proved a preventive and a remedy; it was cheap and practical. *Voila!*

We begin to see how difficult it is to connect cause and effect. People who have an itching place on their skin, or pimples, or an eruption, and who try an advertised salve, may in time effect a cure. The laws of chance would account for that. But the cure also may have come about because they threw away leather garters, or changed their dietary habits, or banished begonias from their living rooms, or for any of a number of other reasons. So long as they do not know the cause of the condition it is ridiculous for them to assert that a variation in any one factor of their varied existence effected an absolute cure.

In 1891 a scientist was studying pear blight, and blight is a modest term for what that does to a pear tree. He produced the disease experimentally by brushing its germs into a number of pear blossoms. These germs multiplied in the nectar and entered the nectaries. But how on earth could the disease, thus entering the blossoms, suddenly affect the whole bloom of a tree? That was a mystery till the scientist watched a bee alight on a pear blossom and suck up the nectar. It then flew to another flower, wiped its feet there, and got some more nectar. Therefore it must be the agent carrying this injurious blight from one tree and from one blossom to another.

SO the scientist got some sterilized test tubes. He caught three bees in the act of sipping infected nectar. He examined them under a microscope and found the disease germs in their mouths. From these germs he developed cultures. The organisms which grew on his cultures were typical pear blight germs because they produced pear blight when inoculated into pear trees. The disease so produced was proved to develope again the same kind of germs, which could again be taken from the nectar of the pear blossoms by the honey bee. The case was proved scientifically and it is that sort of thing I have in mind when I demand scientific proof.

It is a good method to test out the stories we hear about cures and other things for *post hoc ergo propter hoc.* We should ask: Did this cause that? How many factors were varied? How much care was exercised in proving that the factor cited actually did produce the result attributed to it? Do rheumatics who take fake remedies that consist, in the ignorance of the victims, of salts, actually cure themselves of rheumatism, or do they merely feel better because they needed a dose of salts anyway . . . or because the weather changed . . . or their diet changed . . . or because they ceased driving in an open car, or sleeping next an open window . . . and so on and so on?

Scientific proof is most difficult to establish. But it is well worth the effort just the same.

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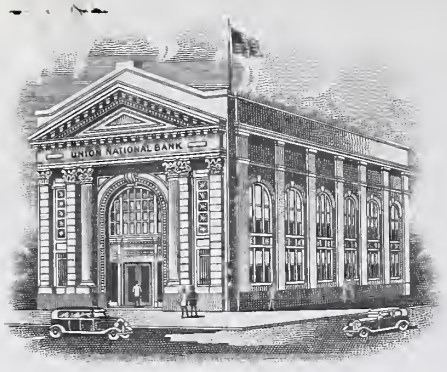


UNION NATIONAL BANK

MACOMB, ILLS.

December 10, 1947

The Lincoln National Life Insurance Co.
Fort Wayne, Indiana

Dear Friends:

I feel like I am under continued obligation to you for your kindness in sending me regularly "Lincoln Lore". The October 6 edition just comes to hand. Your No. 965 is particularly interesting as the writer with his botanical knowledge has been working from ten to fifteen years endeavoring to get our farm population thoroughly aware of the need for eradicating the plant in the fall before it goes to seed and we still have some botanists and others who insist that is is harmless.

A couple years ago our Chemistry Teacher at our Western Illinois State College lost some sheep on his farm and at my suggestion transferred them to another pasture. He brought two stomachs in to his laboratory and found the toxic poison in them.

Would like to have a half dozen of that issue if you have them to spare and will gladly remit you what price is right.

Kindest regards and best wishes of the season.

Yours truly,

L F Gumbart

LFC j

L.F. Gumbart, Vice-President

Special Contribution

Discoverer of the Cause of Milk Sickness

William D. Snively, Jr., MD, and Louanna Furbee

1. White snakeroot (*Eupatorium urticaefolium*).

The season was fall, the year about 1834. The savagery of the southern Illinois backwoods seemed reflected in the wildly beautiful autumnal foliage. Anna Pierce Hobbs, pioneer doctor in the rugged hills of southeastern Illinois, strode into the dense forest covering Hobbs' Ridge.

It was a lovely day to carry on her determined hunt for the unknown killer herb that, she was certain, had been decimating both the human and livestock populations of the pioneer settlement of Rock Creek. Anna had no inkling that, on this day, she would meet the Shawnee medicine woman, "Aunt Shawnee," who would reveal to her the guilty plant. She little thought that she was about to take the last in a series of logical steps that were to lead, inevitably, to her discovery of the cause of milk sickness. Anna's work, reaching its culmination on this day, should have wiped out the vicious scourge that was killing or disabling thousands each year, causing village after village to be abandoned, greatly retarding the settling of the west. Her work should have relegated the milksick plague to the pages of medical history. But it was not to be.

What Is the Milksick?

The record concerning milk sickness, as it has come down to us in the medical literature, is often confused and confusing. So that we can review it with a better perspective (and what perspective excels that provided by hindsight?) let us first summarize what we know concerning the disease.

Milk sickness, usually called milksick by the pioneers, is a synonym for what we now know is poisoning by the white snakeroot. Common in the Midwest and Upper South, the white snakeroot is a member of the Compositae, called *Eupatorium urticaefolium* (Fig 1). It is also called white sanicle, rich weed, squaw weed, snake weed, pool wort, and deer wort. A shade-loving plant, it is frequently seen growing on roadsides, in damp open areas of the woods, or on the shaded north side of ridges. The disease can also be caused, in southwestern United States, by the rayless goldenrod, *Haplopappus heterophyllus*.

Milk sickness has been variously called alkali poisoning, puking fever, sick stomach, the sloes or slows, stiff joints, swamp sickness, tires, trembles (especially in animals) and, more fancifully, caconemia, colica trementia, ergodeleteria, lacemesis, paralysis intestinalis, morbo lacteo, mukosma, and syro. It is also called tremetol poisoning after an identified toxic ingredient of the white snakeroot and rayless goldenrod. Tremetol, obtained from leaves and stems by extraction with ether, is an unsaturated alcohol with the empirical formula $C_{16}H_{22}O_3$. In consistency and odor, tremetol resembles turpentine.

The disease may occur when man or animal eats the leaves or stems of the white snakeroot, or drinks milk or eats butter from an animal that has eaten the plant, or—much less certainly—eats heavily of the flesh or viscera of an animal that has died of acute white-snakeroot poisoning.

The incidence of snakeroot poisoning today is low, yet it is probably higher than morbidity and mortality statistics indicate, since so few present-day physicians are familiar with the disease. The correct diagnosis was not made on two patients seen at the St. Louis Children's Hospital until after they had recovered.[1] It would probably not have been made then, had not the physician in charge seen a patient with milk sickness some years before.

But there is scant question concerning the incidence of the disease in pioneer days. Even allowing for mistakes in diagnosis, milk sickness was probably the leading cause of death and disability in many

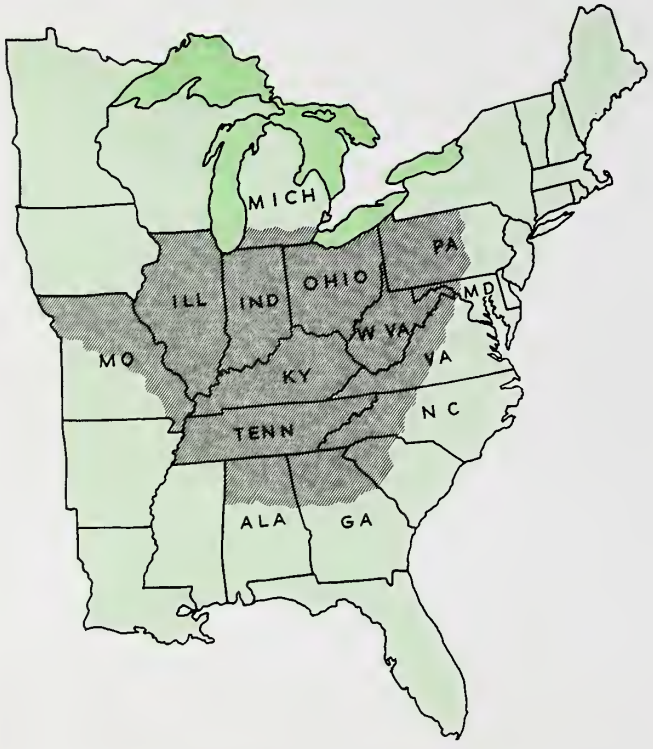
From Mead Johnson & Co., Evansville, Ind, and the Department of Pediatrics, Medical College of Alabama, Birmingham (Dr. Snively), and the American Dental Association, Chicago (Miss Furbee).

Reprint requests to 2404 Pennsylvania St, Evansville, Ind 47721 (Dr. Snively).

communities in the Midwest and Upper South during the 18th and 19th centuries. Its highest incidence was in dry years when cows wandered from their brown pastures into the woods in search of forage. As more forests were cleared so that cattle had more adequate pasture, and as fences were built, the incidence decreased rapidly (Fig 2).

Milk sickness usually occurred in persons who had drunk heavily of the raw milk of a severely poisoned cow. Mixing milk from several cows usually diluted the toxin so that the level in the milk drunk was not high enough to cause the disease. For this reason, little, if any, milk sickness was observed in the populous centers.

The severity of milk sickness is directly related



2. Areas in which milk sickness was reported during 19th century.

to the dose of toxin. Its effects are both intense and widespread. The mucosal lining of the stomach and intestines, the liver, the brain, the kidneys, and the heart show various pathological changes, including hyperemia, cloudy swelling, and fatty degeneration.[2] A severe attack manifests itself as a progressive acidosis that kills within a few days to two weeks, unless vigorously treated. The intensity of the acidosis was shown by the difficulty that Hartmann and others[1] experienced in correcting the imbalance despite the skill of the medical team and the excellent facilities available for diagnosis and treatment. The plight in which the pioneer doctor found himself when confronted with a patient seriously ill with milk sickness can but appall the physician of today.

The disease in animals, chiefly cattle, is called trembles. It is characterized by loss of appetite, weakness, falling, trembling, and stiffness. Abdominal distention develops, and the animals become unconscious. The disease may become chronic, with periods of remission and exacerbation. In man, the symptoms include loss of appetite, listlessness, weakness, vague pains, muscle stiffness, vomiting, abdominal discomfort, severe constipation (called costiveness in the old literature), keto-acidosis, occasionally hypoglycemia and lipemia, and, at last, coma. The severe acidosis produces a characteristic acetone odor to the breath, frequently described in the 19th century literature[3,4] as a peculiar and overpowering fetor. In man as in animals, death can come quickly, or the disease can become chronic and latent. Exacerbations are brought on by fatigue, starvation, intercurrent infection, or vigorous exercise.

Laboratory findings as found by Hartmann and others[1] indicate a profound acidosis. The initial carbon dioxide content in their first patient was 4.5 mEq/liter. Findings in the second patient included a carbon dioxide content of 7.8 mEq/liter and a plasma pH of 7.04. Diagnosis is based on the history of ingestion of milk or butter from a cow that had access to white snakeroot and by acidosis not accounted for by diabetes, salicylate intoxication, or infection. Unless they have an infection, patients with milk sickness have no fever. Those who recover from the acidosis have considerable muscular incoordination and tremors. Hypoglycemia is by no means a constant finding. It was not observed in the carefully studied patients of Hartmann and others.[1] Yet the weakness observed in the disease may be caused, in part at least, by this abnormality.

Recovery from an attack is slow and may never be complete. The lethargy that characterizes the disease has helped give it the name the sloes or slows. In removing McClellan from his command, Lincoln said, "I said I would remove him if he let Lee's army get away from him, and I must do so. He has got the 'slows.' "

Vigorous measures should be directed against the acidosis, with the use of the parenteral route if the patient is unable to retain oral fluids. When the acidosis is intense and resistant, as frequently it is, large doses of alkalis and of carbohydrates may be required to correct it. Whether ethyl alcohol, either as such or in the form of brandy or whiskey, actually exerts a therapeutic effect by neutralizing the tremetol in the body remains open to question, although various physicians have endorsed its effectiveness.[5-8]

The Written Record

Milk sickness appeared in North Carolina as early as the American Revolution,[2,6] where a mountain peak was named Milk Sick. Indeed, the Indians probably knew snakeroot poisoning as a disease of cattle.[9] But the first published account of

the disease was that of Thomas Barbee,[6] who described the new disease in 1809 in *Notices Concerning Cincinnati* without naming it.

By 1811, the disease had a published name, sick stomach.[10] Amazingly, the anonymous author knew as much about the disorder as did most writers for a half century to come. He held that it was a true poisoning, since it involved no fever, and he believed it was caused by poisoned milk, which possessed a singular taste and smell. The source of the poison, he assumed, was vegetation eaten by the cows. The author advised that finding the offending plant would remove a stumbling block to emigration. He noticed that children were less often affected because they immediately vomited the poisoned milk and that horses and cattle kept on cultivated pasture escaped the disease.

On Pigeon Creek in Indiana, milk sickness claimed its most famous victim, Nancy Hanks Lincoln, mother of Abraham Lincoln, during the epidemic of 1818. That Nancy's great-aunt and great-uncle, as well as two neighbors, also died from the disease within weeks reveals the tragic impact of the epidemic. No wonder Dennis Hanks, cousin of Abraham Lincoln, despaired, "We war perplext by a disease cald milksick." Our recent searches near the Lincoln cabin site on Pigeon Creek disclosed a dense stand of white snakeroot.

Only a few articles of moment appeared in the next two decades, although the literature was replete with reports on the disease. Lea[11] in 1821 subscribed to the theory that miasmas caused milk sickness. Parts of a thesis that McCall had written on milk sickness were published, without his direction, in the *Medical and Physical Journal*, with an editor's comment that the existence of the disease appeared improbable. McCall,[5] therefore, wrote a paper in 1823 to clarify his position.

He was convinced that milk sickness was of vegetable origin and that it involved poisoned milk. He also reported that the disease could be contracted by eating the flesh of animals that had perished from trembles. He was one of the first to suggest beverage alcohol as a treatment. Although he had not examined patients himself, McCall included case reports of Dr. M. D. L. F. Sharpe.

The year 1841 brought two erudite publications,[6,11] both of which hindered progress. The famed Daniel Drake,[6] who had not examined a patient with milk sickness, wrote at length on the ailment. Drake discounted the findings of John Rowe, a farmer of Fayette County, Ohio, who, in 1838, announced in a Washington, Ohio, newspaper that he had discovered the cause of trembles in cattle, *Eupatorium ageratoides* (*E urticaefolium*), white snakeroot. He had killed a calf and two cattle by feeding them the plant and a pig by giving it a fluid extract of white snakeroot.[6]

"A professional scrutiny only can be relied on in such cases," wrote Dr. Drake. "The testimony adduced by Mr. Rowe is, therefore, defective and inconclusive." On the heels of this statement, Drake presented some admittedly inconclusive evidence in support of his theory that *Rhus toxicodendron* (poison ivy) might be the cause.

Also in 1841, Seaton[3] published a book on milk sickness, implicating arsenic as the cause. Milk sickness and arsenic poisoning do share some symptoms. The fact that milk sickness occurred more often in dry than in wet seasons seemingly confirmed his belief that the quantity of arsenic was insufficient to poison unless highly concentrated, as in low streams.

A taste for greens led William Jerry[12] to an unexpected discovery in 1867. A day after he ate the leaves of a plant (later identified as *E ageratoides*) that he thought would make excellent greens, he became ill with violent trembling. He reported to the *Missouri Republican* that he had found the plant that causes milk sickness. Mr. Jerry planned to feed the plant to cattle as an experiment, perhaps to win the reward offered some years before by the Legislature of Illinois for discovery of the cause of milk sickness. We found no record that he did so.

Sager,[13] in 1876, subscribed to the theory that the poison consisted of what he termed "low organisms," which live in the soil. In dry seasons, animals grazing on short grass would be more likely to get the disease, hence the higher incidence of milk sickness in such periods.

Sager rejected alcohol as treatment, saying that he relied "on quinine and good nourishment—if it can at all be retained." In the same year, Dumm[7] used alcohol in treating patients with milk sickness, sustaining a 19-year-old boy who had milk sickness by giving him rectal feedings of brandy and milk until the patient was strong enough to take food by mouth. A discussant of a paper by Gardner[8] in 1880 reported that the brandy treatment was his "sheet anchor" 40 years before, and Gardner himself recommended brandy with honey or syrup.

Gardner[8] had begun his search for the cause of milk sickness with an answer: that it was caused by a microorganism. He found an organism resembling "*bacilla subtilissima*" in the blood of a heifer with trembles and in the water source used by the heifer. This finding led him to believe that the microbe was associated with water supplies. He saw one human patient with milk sickness, but she denied him permission to take a blood sample from her.

Three years later, Beach[14] reviewed the theories presented up to that time and stated that he thought milk sickness was an infection. He claimed to have had no failures in patients treated with beverage alcohol and stressed the frequency of the ailment in early years by telling that a quarter of the pioneers in his home county of Madison, in Ohio, had died of it.

The definitive work on milk sickness was not published until 1941,[4] but its author, Moseley, had written voluminously throughout the early

20th century. Moseley was the foremost proponent of the white-snakeroot-poisoning theory. In careful feeding trials, he established the toxic dose of snakeroot for animals at 6% to 10% of body weight. He reported the stems less poisonous than the leaves and declared that neither freezing nor drying destroys the poison.

According to Moseley, a common veterinary remedy was large doses of soda. He reported that buyers frequently forced stock to run before purchase to make the latent disease manifest.

Moseley's opponents were several, among them Crawford[15] of the US Department of Agriculture, who rejected Moseley's positive findings concerning white snakeroot. Crawford even rejected his own positive findings, and has been criticized by many since for his lack of objectivity: Of six rabbits fed or given injections of white snakeroot, three died, and two showed symptoms of the disease; the only one unaffected was lactating. Interestingly, Crawford seems not to have had a pet theory himself, although he suggested a night organism might be a carrier of a parasite responsible for the disease.

In 1909, Jordan and Harris[16] published the foremost argument for the microbe theory in a monograph on a microorganism they isolated and believed the cause of milk sickness: *Bacillus lactimorbi*. Several pictures of *B lactimorbi* are included in their report and, based on examination of these and of the detailed culture data given, *B lactimorbi* apparently consisted of two genera of bacteria, a *Corynebacterium* and a *Bacillus*. An extensive series of experiments appeared inconclusive.

Luckhardt's study[17] was an extension of that performed by Jordan and Harris[16] to establish *B lactimorbi* as the cause of milk sickness. Despite his close association with Jordan and Harris, Luckhardt advanced a guarded opinion regarding the microbe: "The preceding experiments are, I believe, far from being decisive in establishing *B lactimorbi* as the etiologic factor in the production of milk sickness." The experiments involved inoculation of six dogs with *B lactimorbi* organisms; two showed slight symptoms similar to those in milk sickness; one of these two died.

At last, in 1928, white snakeroot was established with certainty in the literature as the cause of milk sickness. In that year, Couch[18] reported isolation of three poisonous substances from the plant, a volatile oil and a resin acid that do not produce trembles and an oily liquid with the characteristics of a secondary alcohol that does cause trembles. The last he named tremetol.

Tremetol gives a color reaction with concentrated sulfuric acid, but the test is not entirely reliable. Probably milk secreted by tremetol-poisoned cows contains a metabolized product of tremetol, also poisonous, rather than tremetol. Couch reported that tremetol disappears from the plant when it is dried, a finding in disagreement with that of Moseley,[4] who wrote that the dried plant was toxic.

Not until the careful work of Hartmann and others[1] in 1963 were the importance and seriousness of the acidosis accompanying milk sickness fully recognized.

In reviewing the written record, we are struck by several peculiar facts. Few authors observed the characteristic fetor of the breath, an important diagnostic sign of milk sickness. Surprisingly few actually examined patients who had milk sickness. Throughout the literature, authors have tended to locate the ailment in the organ from which symptoms seemed to originate. For example, anorexia and vomiting, really caused by systemic acidosis, gave the disease its names, sick stomach and puking fever. Most authors approached their studies with fixed conclusions, then discarded evidence that did not support their pet theories, an error easily made since valid clues frequently were applicable to more than one theory. Also, the nature of the opinions was strongly influenced by the medical fashions of the times.

An Epic Discovery

At age 16, Anna Pierce came west from Philadelphia with her family in an ox-drawn covered wagon. Descending from the mountains into Kentucky, the Pierce family drove westward to cross the Ohio River into Illinois at Ford's Ferry in 1824. They carved a farm from the wilderness just north of what later became Rock Creek, in southeastern Illinois.

Disturbed by the sad state of the health of the pioneers, Anna determined to become a physician. She returned to Philadelphia to take courses in nursing, midwifery, and dental extraction, all the professional education available to her since medical courses were not generally open to women in those days. About 1828, she returned to Rock Creek to minister to the medical needs of the community (Fig 3).

As the only health practitioner in southeastern Illinois, Dr. Anna—as she was called—coped fairly well with the ailments of the frontiersmen, until an epidemic of a strange disease ravaged the settlement (Fig 4). Not long after the onset of the epidemic, Dr. Anna, who appears to have been an excellent observer, noted that the men and animals that contracted the disease had been drinking milk. Her biographer, E. N. Hall,[9] stated that she gave the disease the name milksick, but actually earlier reports had used the term.[5,11]

Anna's deep concern with the highly fatal disease, the course of which seemed to have been little affected by her treatment, became even more acute when the ailment killed her mother and her sister-in-law, Mary Hobbs, and made her father seriously ill. Still suffering from the disorder's aftereffects, Mr. Pierce returned to Philadelphia, where he hoped to obtain treatment that would help him recover his health. He took Anna's brother, George, and George's daughter Abigail with him.

Sometime before the epidemic of milk sickness, Anna had married Jefferson Hobbs, an esteemed farmer and lay preacher. The two settled on a farm about a mile from the original Pierce homestead, where they continued to live after the rest of the Pierces returned to Philadelphia.

After ascertaining that the disease was caused by drinking milk or eating butter, Anna made a second excellent observation. She noticed that the ailment was seasonal, beginning in June and ceasing soon after the first frost. Then she observed that, although both men and animals were dying of the disease, milk cows appeared not to contract it, until after those that had drunk the milk had sickened and, perhaps, died. Anna wrote in her diary: "I am convinced now that the poison which kills the calves and people saves the cows by being daily discharged through the milk glands. So I am writing a few letters this morning and telling everyone I can to abstain wholly from milk and butter from June till after killing frosts."[9]

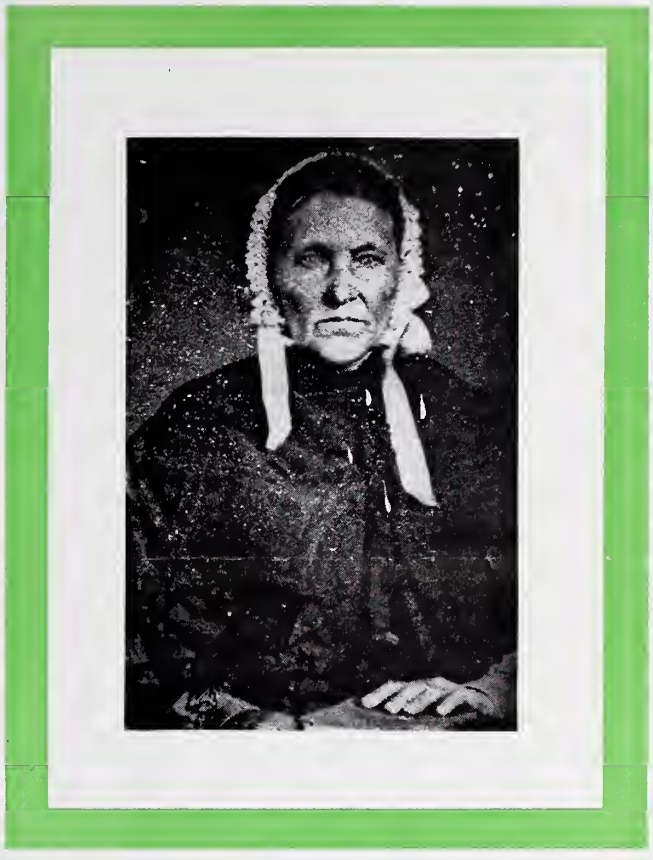
Next, Anna observed that horse, sheep, and goats did not develop milk sickness to any extent. From this, she concluded that an herb was responsible for the disease, reasoning thus: "Sheep and goats are careful in selecting their foods, and horses are what teachers call graminivorous; that is, grass-eaters, while cattle are herbivorous and not careful in selecting. These things prove to us that it is not a grass, but an herb that is spreading sorrow and death among us."

Then, on that eventful fall day, Dr. Anna packed a frugal lunch, took rifle and dogs for protection, and, carrying her herb basket, followed the cattle into the woods that bordered Rock Creek. All forenoon she trailed after them, as she had so many other times, picking specimens of the herbs on which they fed.

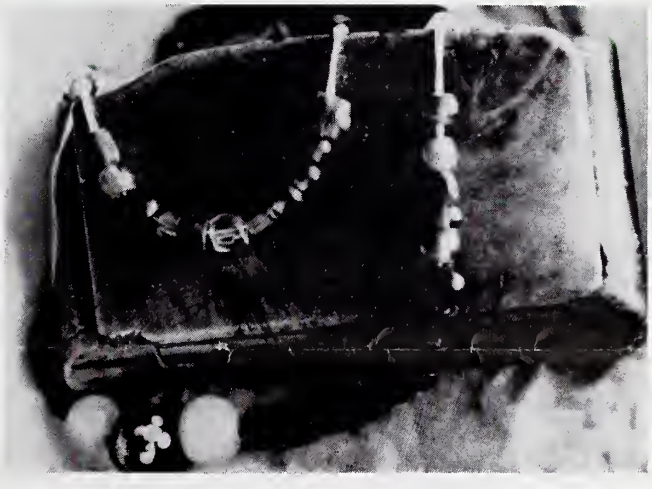
About noon she saw an Indian squaw hiding in the underbrush. Anna called to her kindly. When the squaw came from hiding, Anna was delighted to find that the old woman was an Indian medicine woman, a fugitive from a forced migration of Shawnee Indians west. Anna gave the hungry squaw her lunch and took "Aunt Shawnee" home with her.

Two days later, the old woman, learning of Anna's interest in the disease milk sickness, led her to the north slope of Hobbs' Ridge where she pointed out white snakeroot plants and said they were the cause of trembles and milk sickness. She told Anna that the plant was well known to the Shawnee, since they used its root as a remedy for snakebite. Anna gathered a basket full of white snakeroot and, deeply gratified, went home. Her husband fed several bunches of the herb to a calf, which developed typical trembles. His experiment reinforced Anna's conviction that she had indeed found the cause of milk sickness.

Anna started an ambitious snakeroot eradication program. She encouraged men and boys to search the woods and fields, uprooting and burning all white snakeroot. Through summer and fall, the program went forward for three years. At the end of the period, the weed and the disease had been virtually eliminated from southeastern Illinois. (A search we carried out during the fall of 1965 revealed that the white snakeroot is again extremely prevalent in southeastern Illinois.) So that doctors from neighboring communities might know white snakeroot, Anna grew a patch of it in her garden and wrote letters inviting physicians in the nearby regions to come and examine the plant.



3. Anna Pierce Hobbs Bixby in her later years.



4. Dr. Anna's "blood beads" and handmade leather case. Blood beads were believed to stop hemorrhage when placed around the neck.

The second winter after Dr. Anna had discovered the cause of milk sickness, Jefferson Hobbs died of a virulent form of pneumonia, then epidemic. Anna was immensely distressed by his death, but she carried on her work of mercy. In addition, she founded and was active in the Rock Creek Church, which is still in existence. Some years later, she married a young ne'er-do-well, Eson Bixby. The marriage was unhappy, and Anna separated from her husband. Later Anna was to have many exciting adventures, which have been recorded by E. N. Hall.[9] Throughout them all, Anna continued to serve Rock Creek as its only physician. She died in 1869, having received no recognition for her remarkable discovery.

The question is inevitably raised, "Why did it take the medical profession as a whole so long to discover the cause of milk sickness?" The answer has many facets: (1) The occurrence of milk sickness was sporadic, making serial observations difficult. (2) Numerous species of snakeroot, similar in appearance, vary greatly in toxicity. (3) Milk secreters escape poisoning early. (4) The widespread belief in miasmas as a cause of disease led many to believe that miasmas caused milk sickness. (5) Milk sickness superficially resembles arsenic poisoning. (6) Nonprofessional people, like John Rowe, though excellent observers, were held in disdain. Physicians, like Dr. Daniel Drake, though rigid and opinionated, were held in awe. (7) Confusion was caused by the belief that that disease could be contracted by eating the flesh and entrails of animals dead of trembles. (8) The medical profession lacked such elementary diagnostic aids as a reliable clinical thermometer, hence could not readily distinguish between a toxicosis and an infection. (9) Physicians had inadequate training in the scientific method; many were not even good observers. (10) The white snakeroot was sometimes infected with a bacillus, also found in some persons with milk sickness. Although the bacillus was shown to be nonpathogenic, for a time some believed it to be the cause of milk sickness. (11) There was a lack of consistent, sustained medical communication. Medical journals, societies, and meetings as we know them today were in a primitive state of development, especially in the backwoods areas. Hospitals, where physicians could meet and exchange ideas, were nonexistent. (12) Because the disease was limited to the Midwest, Upper South, and West, some influential eastern physicians believed it did not even exist.

The above factors, which combined to confuse anyone trying to discover the cause of milk sickness, constitute a formidable list. Perhaps we should not be too surprised that some of the most distinguished physicians of the day were completely misled. But we can well be amazed that these same sources of confusion did not divert Dr. Anna from the straight path of accurate observation and logical reasoning that led her, inadequately trained and isolated as she was, to the cause of the terrible plague. Consider in summary her accomplishments: She discovered the cause of the disease and reproduced it in animals at least four years before farmer John Rowe's[6] report; she carried out the first thorough white snakeroot eradication program; she anticipated official medical recognition of the cause of the disease by nearly a century. Clearly she must have been a woman of rare talents and unusual dedication. She deserves, at this late date, a full measure of honor and respect.

Thomas S. Acker, SJ, PhD, John W. Allen, L. A. Dearinger, Ivy K. Joyner, Betty Lou Keenan, Walter Page, J. D. Quarant, and Gertrude Tyer assisted with the research on which this paper is based, and Arthur N. Bahn, PhD, interpreted the putative microorganisms.

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Fort Wayne Journal Gazette, Sunday, Sept. 3, 1967

This Weed Changed Course Of History

A public service feature of ACRES, Inc., dedicated to the preservation of natural areas in Northeastern Indiana.

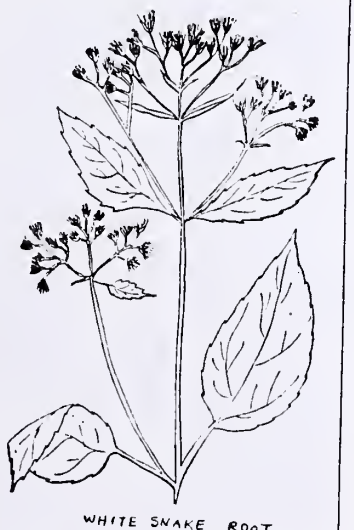
By JOHN W. KLOTZ
Professor Of Biology
Concordia Senior College

Life on the frontier was always hard and precarious: The pioneers were surrounded by dangers on all sides. To fell the trees, to coax crops, to build log cabins and barns, to care for livestock, to make or improvise for most of your necessities took men and women of courage and not a little stubbornness.

Tom Lincoln had these qualities. He had moved his family from Kentucky to Indiana late in 1816 and had settled along the Little Pigeon Creek in what was then Hurricane Township of Perry County near Troy: shortly thereafter it became Carter Township of Spencer County. It was real frontier living with all the pleasures and hazards of a newly inhabited area. Not the least of the latter was milk sickness, a mysterious disease which was first reported from North Carolina and which seemed to follow the pioneers as they moved through the central states. So devastating was the disorder that in some places the original population was reduced to less than half its original number in just a few years. On some occasions whole villages were abandoned because it was soon discovered that milk sickness was endemic to only certain limited areas.

No one really knew what caused it. Some said it was due to poison ivy that caused severe itching and discomfort in those susceptible to it. Others spoke of mysterious miasmas rising from the soil or from spider webs. A great many were convinced that it had some relationship to milk and so it was generally known as milk sickness. Some suggested that the water supply of the cattle was contaminated by arsenic, cobalt, copper, or lead.

But no matter what the cause, it was destined to play an important role in the life



WHITE SNAKE ROOT

of Tom Lincoln and his family. In the fall of 1818 one of his cows came down with the "trembles," an ominous sign indeed. Then Thomas Sparrow, husband of his wife's aunt, was stricken and failed rapidly. That he was dying was readily apparent. He made his will, leaving all his property to his wife; Nancy Hanks Lincoln was one of the witnesses to the instrument. Mrs. Sparrow survived her husband by only a few weeks; she also succumbed to the mysterious malady. Not long thereafter, another neighbor, Mrs. Peter Brooner, was stricken, and at the time of her death Nancy Hanks Lincoln was herself showing some of the symptoms. Seven days after she was first stricken, Abe Lincoln's mother died on Oct. 5, 1818, leaving behind her husband Tom, a daughter Sarah, age 11, and young Abe, who was only nine.

Milk sickness was indeed a strange disease. Most disorders are characterized by a fever, but with milk sickness the victim has no temperature whatsoever: indeed his temperature may be below normal. The symptoms are a general weakness, nausea, and prostration. The victim shows a reluctance to move; his whole behavior is sluggish. A day or two later his appetite disappears; he experiences abdominal pain and nausea. Severe, repeated vomiting follows; there's also an obstinate constipation and a severe thirst accompanied by repeated drinking and then loss of the water by vomiting.

The same muscular tremors that characterize the disease in animals follow. As the disease progresses there is a characteristic odor of acetone on the individual's breath and this may be followed by delirium, coma, and death. The mortality ranged between 10 per cent and 25 per cent. In those people who are spared, the recovery is slow and uncertain. Relapses are frequent following even moderate exertion and these relapses may terminate fatally. Individuals were often incapacitated for several years following an attack or, in some cases, were permanently disabled.

What really caused the disease? It reached its peak in the early nineteenth century, but continued to be a problem for several decades in the last part of the century. When germs were discovered, an attempt was made to link milk sickness to some micro-organism, but it was soon apparent that this was not a germ disease. One thing continued to be clear; it was associated with milk and transmitted to human beings through milk and milk products.

Finally after much careful study, the culprit was identified, a common plant, widespread over most of the United States, the white snakeroot. The toxic substance is a thick, straw-yellow oil with an aromatic odor called tremetol. Tremetol occurs in the plant in combination with a resin acid which probably exerts a toxic effect itself or intensifies the effect of the tremetol. Ingestion of the plant by animals results in the trembles: the animal doesn't want to move and shows a stiffness in walking. When standing, he stands with his feet apart and begins to tremble especially about the flanks and hind legs. The trembling becomes increasingly severe and is often fatal to the animal. The disease has been produced experimentally in sheep, cattle, horses, hogs, and human beings. Suckling animals get it from milk and may show it even before their parents.

Tremetol is excreted only slowly and therefore accumulates in the bodies of animals taking it in. The toxicity seems to decrease with drying; still, dry white snakeroot hay produced trembles in an animal six months after it was cut.

White snakeroot is a common perennial and is in bloom right now. Ordinarily it grows from one to four feet tall. The leaves are opposite. They're thin, coarsely and sharply toothed, from three to six inches long, heart-shaped with the apex of the heart drawn out into a long point. The flowers occur in a loose cluster of small heads, each of which has from ten to thirty bright white, tubular flowers. The

"A Disease Cald MILKSICK"

By DAN SNIVELY, M. D.
and
JAN THUERBACH

THE SUMMER of 1818 had been fearfully dry, the lush meadow grass of southern Indiana burned brown by the forge-hot August sun. Relentlessly the drought dragged on through September and into October. As the pioneer woman gazed over the withered clearing near her cabin a giddiness seized her. She felt nauseated. "Milksick?" she wondered, then tried to dismiss the frightening idea. It *was* the season for the milksick and the plague *had* struck the settlement heavily. Within the past few weeks the woman's aunt and uncle and a neighbor died of the ailment.

Next morning when the woman arose she had no appetite and her dizziness and nausea were much worse. Her legs ached and she shivered as if wintry blasts were already blowing. Her husband, 11-year-old daughter, and 9-year-old son looked at her apprehensively. The husband would have ridden for the doctor had there been one in the area. There was none. Next day the woman began vomiting, her head started aching, and she took to bed.

The sixth day of the illness, just before her mind started to wander, she called her children to her, stroked their tear-streaked faces and made them promise to look after their father. From then on her course went steadily down and before the end of the second week she succumbed and joined her relatives and neighbor in the little cemetery over the hill. With trembling hands her young son had whittled out the pegs that held the whip-sawed planks together for his mother's coffin. Nancy Hanks Lincoln, dead of the milksick, would not know of the great destiny that lay ahead for her son Abe.

TO THE pioneers it always seemed that the milksick struck without warning, appearing unheralded in the community like a miasma that had drifted in from the swamp—which was exactly what some physicians thought it was. Persons with a "bad case" usually died within five days to two weeks. Very few survived. Some areas lost a fifth of their population to the milksick over the span of a few years. A terror spoken of only in whispers, the milksick was regarded as such a blight on a community that its presence was always denied. "The milksick here? Never!" Up the river, maybe; in the next valley, maybe; in the town over the ridge, maybe. Never here!

Pioneer observers wrote:

"Perhaps there is no disease [occurring with] such frequency and accompanied with such fatal results as milk sickness."

"No wonder pioneer families by whom malaria and typhoid were accepted as a matter of course fled back east in terror from this mysterious disease from which . . . [settlers] died so suddenly."

"The Thomas family, our new neighbors, lost their tiny children in September—victims to that most welcome of all childhood's nourishment—a draught of sweet milk."

"Danville, Indiana, has now become a perfect charnel house. No less than fifty died of milksick during the past year, and that too out of a population of 500 inhabitants."

"More than half of the deaths that occurred in the early 19th century in Du-Bois County, Indiana, were said to have been caused by milk sickness."

Exceeding the ever-present malaria and the catastrophic cholera as a killer of pioneers, the milksick reared its hideous head nearly every summer and fall, striking most ferociously in drought years. It drove terrified pioneers from countless settlements in the Midwest and Upper South: a map portraying the departures would be dotted with villages that are no more. Discouraged by the ever-recurring disease, the Lincolns departed the lush hills of southern Indiana for Illinois. Abe's cousin, Dennis Hanks Lincoln, explained the move years later: ". . . we war perplext by a Disese cald Milksick . . . I was determed to Leve and hunt a Cuntry whare the milk[sick] was not [present] . . . we Riped up Stakes and Started to Illinois."

IT SEEMED strange that milk sickness did not appear until the pioneers began settling west of the mountains—never in the early colonies along the Atlantic seaboard, nor in Europe, nor on any other continent. It was seen in North Carolina as early as the American Revolution, where a mountain peak was named Milk Sick, but the first official report was not made until 1809 when Dr. Thomas Barbee described the new disease that he had observed on a visit to the Mad River country of Ohio.

In 1811, an anonymous author wrote about the ailment, calling it "sick stomach." Amazingly, he knew as much about the disorder as did most writers for a half century to come. He said it was a true poison-

American History Illustrated
July 1970

The death of Nancy Hanks Lincoln, a victim of milk sickness. From the drawing by Lloyd Ostendorf. (Courtesy of the artist)

ing, since it involved no fever, and he believed it was caused by poisoned milk, which possessed a singular taste and smell. The source of the poison, he assumed, was vegetation eaten by the cows, and if the offending plant could be found, the disease could be eradicated.

Not until 1928 was the cause of the disease established with certainty although a pioneer lady doctor in Illinois and a farmer in Ohio had both, unknown to one another, pointed out the correct cause nearly a century before. Their assertions were either disputed or totally ignored. A pretty flowering weed with the faint aroma of lilacs, called the white snakeroot because the Indians treated snake bites with its root, was the culprit! Cows that ate the weed secreted its deadly poison, tremetol, into their milk and both human beings and calves drinking of that milk suffered its lethal effects.

White snakeroot, or more precisely *Eupatorium urticaefolium,* is also called white sanicle, rich weed, squaw weed, snake weed, pool wort, and deer wort. A shade-loving plant, it grows frequently on roadsides, in damp open areas of the woods, or on the shaded north side of ridges. The disease can also be caused, in southwestern United States, by the rayless goldenrod, *Haplopappus heterophyllus.* Various species of white snakeroot appear similar but vary greatly in toxicity. This is the reason milk sickness occurred only in certain regions. Delay in identifying it as the definite cause of milk sickness can also be attributed to this variation in the plants.

THE incidence of milk sickness decreased sharply as farms were created from the wilderness, pastures fenced, and cattle kept from grazing in the woods where most snakeroot grew. Modern methods of milk purification have practically eliminated the disease, although cases were treated as recently as 1963. It still occurs when people drink raw milk from cattle that have grazed in woods where white snakeroot grows.

Dr. Mark Greer, still practicing in Vandalia, Illinois after more than half a century, told us of a family he treated in 1921. The mother had died two days earlier, a 16-year-old girl lay in a coma, and two boys were seriously ill. The father and two other boys had just recovered from mild attacks. Dr. Greer recognized the symptoms of milk sickness. Next morning the girl died; the boys recovered but for months became exhausted at the slightest exertion.

The pioneers called this sluggish aftereffect of milk sickness "the slows." Many a man who had recovered from the disease was heard to say, "I was never the same after I had the milksick." Abraham Lincoln used the term when Montgomery protested the removal of McClellan from his command: "I said I would remove him if he let Lee's army get away from him, and I must do so. He has got the 'slows,' Mr. Blair."

Still in some respects a "riddle wrapped in a mystery inside an enigma," to use Churchill's description of a quite different sort of puzzle, the strange story of the milksick must fascinate the student of history since it has played such a key role in shaping our early destinies. Years ago Southerners erected a monument to the boll weevil, that deadly plague of cotton. Perhaps the "disease cald milksick" also deserves a monument—for, who can say, without it the path that Abraham Lincoln walked to the Presidency might have been an entirely different one.

Dr. Dan Snively is a prolific writer of articles on medicine and medical history for several journals, and a former executive with Bristol-Myers. Jan Thuerbach has worked with Dr. Snively on several occasions, and with him co-wrote "Sea of Life."

THE MARY IMOGENE BASSETT HOSPITAL

COOPERSTOWN, N. Y. 13326 · TEL: (607) 547-6011

December 28, 1979

Mr. Mark Neeley
Director
Lincoln Library and Museum
1300 S. Clinton Street
Fort Wayne, Indiana 46801

Dear Mark;

This letter serves as a belated follow-up to my visit to the museum in April of this year with Dick Toft. I have pursued the topic of "poisonous white snakeroot" and found it a fascinating one. Enclosed are a few summaries of the information on the drug. Apparently it was quite a common intoxication in pioneer days. The medical aspects are not entirely clear to me yet; the intoxication is unusual in that it is slow in onset yet causes profound metabolic derangements. I am attempting to get more data on the physiology of the intoxication.

I would be very interested in combining our interests into a small paper on the role of this poison in the shaping of Lincoln's eventual career. From a historical and medical viewpoint I think such a paper would be well received in the medical literature. If you would be interested drop me a line and we can discuss the idea more.

Sincerely,

Bill Streck

William F. Streck, M. D.

WFS:sjc

Thienes, C.H. Clinical Toxicology. 5th ed. Lea & Febiger, 1972

necessary. If blood pressure is low, efforts to raise it should be by means of intravenous infusions, raising the foot of the bed, binding of limbs and maintenance of body temperature. Neither norepinephrine nor epinephrine should be used, since these vasopressor agents, in the presence of halogenated hydrocarbons, may cause marked cardiac arrhythmia and even ventricular fibrillation. Mephentermine, methoxamine, phenylephrine or methylamphetamine may be tried, with caution.

For cardiac failure, cardiotonic glycosides are sometimes of value. In less critical situations, digoxin or digitoxin may be given by mouth; in an emergency, ouabain or lanatoside C may be given intravenously.

Renal failure may be noted by the second day. At the beginning of albuminuria or oliguria, efforts to reduce renal edema should be instituted: 50 Gm of mannitol in 250 to 500 ml of water should be infused over a 6-hour period, then 25 Gm every 6 hours for 5 days, unless complete anuria develops. Complete anuria may require peritoneal or vascular dialysis until recovery of the function of the kidneys.

An effort should be made to prevent necrosis of the liver cells as soon as the diagnosis is made. Dextrose should be given orally in a dose of 10 to 20 Gm every 4 hours, or as the 10% solution intravenously at a rate of 200 Gm per day for 1 to 3 days, or longer if renal function persists. Calcium chloride or calcium gluconate, as the 10% solution, should be given intravenously in a dose of 1 Gm every 4 to 8 hours, or as the lactate orally, 1 Gm every 4 hours. Vitamins of the B-complex should be given orally or by intramuscular injection in therapeutic doses once or twice daily. If hepatic necrosis occurs, the same treatment should be given. Methionine is thought to be of value as is arginine glutamate in combatting the accumulation of ammonia and 25 Gm of the latter may be added to 500 ml of 10% dextrose solution (see page 258). Such treatment may be used also for patients with hepatic failure due to cirrhosis; but in both instances, the administration of arginine glutamate has been questioned.

MILK SICKNESS (TREMBLES)

(Richweed, Rayless Goldenrod)

Milk sickness is variously called alkali poisoning, caconemia, colica trementia, ergodeleteria, morbo lactes, mukosma, paralysis intestinalis, puking fever, sick stomach, sloes or slows, stiff joints, swamp sickness, syro, tires, and trembles.

Dr. Anna Pierce Hobbs in 1834 was shown the white snakeroot in the forests of Southern Illinois by "Aunt Shawnee," a Shawnee medicine woman.

John Rowe, a farmer, in 1838 made the first public announcement that white snakeroot is the cause of trembles. Dr. Daniel Drake in 1840 failed to confirm Rowe, and the matter remained in doubt until 1917 when tremetol was isolated by the Bureau of Animal Industry of the United States Department of Agriculture. Nancy Hanks Lincoln is said to have died of snakeroot poisoning in 1819.

Toxic Dose. The toxic dose is not known.

Source and Chemistry. An aromatic, optically active, straw colored oil, tremetol, occurs in richweed or wild snakeroot (*Eupatorium urticaefolium* or *ageratoides*) and in rayless goldenrod (*Aplopappus heterophyllus*). In consistency and odor, tremetol resembles turpentine. The weed is now called by many names: deer wort, pool wort, richweed, snake weed, squaw weed, and white sanicle.

Absorption. The material is absorbed from the mouth, alimentary canal and other mucous membranes and from abraded skin.

Etiology. The disease in humans is due to the eating of the plant, and probably more frequently from the consumption of milk products or the flesh of poisoned animals. Animals are poisoned by eating the plant, or by eating the flesh of other poisoned animals.

Symptoms and Actions. Symptoms in man usually begin as a sense of fatigue and pain, stiffness and weakness of the legs. Anorexia,

nausea and vomiting, distress and prostration soon follow. The tongue is red and the temperature and blood pressure are low. An odor of acetone on the breath is prominent. Consciousness may be lost. The symptoms often continue for several days. Relapse is frequent, and death may occur during the first acute illness or after a relapse. In patients who recover, marked weakness persists for 1 to 3 weeks.

Acetone is present in excessive amounts in blood and urine, the blood sugar is usually low, there is a retention of nitrogenous waste products in the blood and in experimental animals guanidine (normal 0.4 to 8 mg per 100 ml) reaches 6 to 9 mg per 100 ml before death. Acidosis is a constant finding.

The exact mechanism of action is not well understood, but at autopsy, marked liver and kidney degeneration are seen, and it may easily be that the damage to these organs is responsible for the chemical changes in the blood. The hypoglycemia resulting from liver damage can account for the sense of weakness, and the acidosis for many of the other symptoms. On recovery, great hunger is experienced.

In animals, trembling is uniformly seen and this symptom is responsible for the term "trembles" attached to the disease.

Duration. Symptoms develop within a few hours after poisoning and may continue for days. Death before the end of the second day is rare. Where a poisoned milk supply is in continual use, symptoms have persisted for several weeks.

Fate and Excretion. Little is known of the fate or excretion of tremetol, except that it appears in the milk of poisoned animals.

Pathology. Liver, kidneys, pancreas and sometimes other organs exhibit fatty degeneration.

Diagnosis. A history of eating the plant, or of the consumption of milk products or meat of poisoned animals is essential for the diagnosis. Diabetes and acidosis of other origin (dietary, renal, infection) must be ruled out. The poisonous principle can be chemically identified in milk.

Cause of Death. Hypoglycemia, acidosis, or other effects of liver and kidney damage cause death.

Treatment. Evacuation of the stomach is rarely of value, in view of the latent period between ingestion of the poison and the development of symptoms. Measures to combat the hypoglycemia, acidosis and hyperguanidinemia consist of the administration of carbohydrates (glucose, corn syrup), alkalies such as baking soda, other electrolytes and calcium salts. Cutler recommends intravenous administration of calcium salts as an antidote for the hyperguanidinemia. Hardin reported that alcohol, given to the point of intoxication is of definite value. Mountaineers traditionally treat milk-sick with brandy and honey. In view of current concepts, alcohol treatment seems irrational.

If the ammonia of the blood is increased, infusion of arginine glutamate, by intravenous drip of 25 Gm in 500 ml of 10% dextrose, is recommended.

PHOSPHORUS

Toxic Dose. One half Gm of yellow (or white) phosphorus has a 16% and 1.5 Gm, 95% mortality. As little as 15 mg may produce symptoms, and death has occurred with 100 mg.

Absorption. Yellow phosphorus is slowly but nearly completely absorbed from the intestine, requiring bile or fats for its solution.

Etiology. Phosphorus poisoning was formerly frequent among children due to eating match heads containing the yellow form. Such matches are no longer available in the United States. Such poisoning also occurred in children during the late nineteenth and early twentieth centuries from the therapeutic use of phosphorus in the treatment of rickets. In recent years phosphorus poisoning occurs chiefly from ingestion of rat poison. Red phosphorus is insoluble and non-absorbable, and hence nontoxic by mouth, unless contaminated with the yellow form. The vapors of phosphorus have produced poisoning when inhaled.

Eupatorium urticaefolium

Eupatorium urticaefolium (richweed, white snake root, poolwort, poolroot, white sanicle, deerwort, squaw weed) and *Apolapappus heterophylus* (rayless goldenrod) are natives of the eastern and western United States. *Eupatorium* contains an unsaturated alcohol, tremetol, which is responsible for the toxic effects of the plant. These are usually called collectively "milk sickness" because the disturbance results from the ingestion of milk from cows which have eaten the plant. Poisoning was very common in the pioneering era, but is at present less frequent because with progressive cultivation of pasture land the plant has become less abundant, its habitat being mainly woody sections. The onset of the poisoning is gradual and is characterized by fatigability and loss of appetite. After one or two days the patient develops severe and persistent vomiting associated with obstinate constipation, abdominal distress, oliguria, severe prostration, stiffness of the legs, and trembling. The patient's breath has a characteristic acetone-like odor. He has no fever, but rather a lowering of the body temperature; he suffers from great thirst, becomes restless, later somnolent, and comatous shortly before death. The pupils react sluggishly, the conjunctiva may be inflamed, the pulse is irregular and rapid, the blood pressure low, and the respiration irregular and sometimes of Cheyne-Stokes character.

TREATMENT. Treatment consists in the administration of saline cathartics, alkali until the urine turns alkaline and enemas with a 5 to 10 per cent solution of sodium bicarbonate. A diet low in fat has been suggested.

Clay, A. J.: Illinois Med. J., 26:103, 1914.
Walsh, W. E.: J.A.M.A., 87:555, 1925.

Faba bean

Faba vulgaris (Windsor, or broad bean) belongs to the legume family. The inhalation of its pollen or the ingestion of the green undried bean, or of beans which are not well cooked, causes favism, characterized by icterus, hemoglobinuria, and severe anemia. The disease is very common in the Mediterranean countries, and in recent years it has also been observed in this country; the rate of fatalities is said to be 8 per cent. The disease sets in suddenly with dizziness, followed by vomiting and diarrhea and severe prostration. Within a few hours to one day hemoglobinuria develops, the urine turns red-brown to black, the skin turns livid because of anemia, and icterus develops. This is associated with enlargement of the liver and spleen, and often also with dilatation of the heart. In some cases there is a marked increase of the nonprotein nitrogen level in the blood. The disease is probably of allergic nature.

TREATMENT. This consists of prompt transfusion of blood, of dextrose solution, or of isotonic saline, the administration of ascorbic acid, and in

Streck

January 25, 1980

William F. Streck, M.D.
The Mary Imogene Bassett Hospital
Cooperstown, New York 13326

Dear Dr. Streck:

I read your letter and enclosures with great interest. The idea of collaborating on a note or article about milk sickness is very appealing. All I could do, of course, is compile the historical evidence that Nancy Hanks Lincoln died of the disease and search the literature for general references about "epidemics" of the disease. I can suggest possible places for publication as well, though you may have medical journals in mind.

It is too bad that the Lincolns weren't heavy drinkers. It sounds as though it might have saved Nancy's life.

If you still wish to do this, let me know. We'll set a deadline and get to work.

Sincerely yours,

Mark E. Neely, Jr.

MEN/jaf

The "Slows"

The Torment of Milk Sickness on the Midwest Frontier

WALTER J. DALY

In the early nineteenth century, as white settlers flooded onto the midwestern frontier, a new and highly fatal disease appeared among them. The sickness was unknown along the eastern coast and elsewhere in the world. Settlers were forced to guess at its cause and attempt to treat it without benefit of prior experience or modern clinical research. An understanding of the disease's pathology and the discovery of a successful treatment had to wait until the advent of twentieth-century biochemistry. By that time, milk sickness had almost disappeared, and today it is nearly forgotten.

Walther J. Daly, M.D., is dean emeritus of the Indiana University School of Medicine at Indianapolis. In the *IMH* he has previously published "The Origins of President Bryan's Medical School" (December 2002).

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WHITE SNAKEROOT
(Eupatorium urticaefolium)

Courtesy New York State Museum
Albany, N. Y.

White Snakeroot